DEMENTIA: A 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." In recent years, however, there has been an increased awareness, and 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, 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, which will cause 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. This report seeks to present an overview of dementia and the burden it increasingly is imposing on the State of West Virginia.

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.

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.

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, depression, or certain tumors; these, however, account for only about 20% of all dementia (1). The majority of dementias are irreversible.

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. It is estimated that 50% of primary caregivers develop marked emotional distress (2). While many dementia patients live in long-term care (approximately one-

half of nursing home residents suffer from dementia [3]), that represents just a small proportion of persons with dementia. From two-thirds to 95% (4) are cared for at home 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 50% to 70% of all dementia cases (5). Early-onset AD, which develops before the age of 65, is relatively rare, accounting for less than 10% of all AD patients (6). 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.

Alzheimer's disease (AD) is by far the most frequently diagnosed form of irreversible dementia, accounting for 50% to 70% of all dementia cases.

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.

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Vascular dementia is the second most frequently diagnosed type of dementia. It is estimated that it comprises from 10% to 20% of all dementia, and is mixed with AD in another 20%. 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 damage from TIAs can cause what is termed **multi-farct 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 (7).

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.

PREVALENCE OF DEMENTIA

It is estimated that as many as seven million people in the United States suffer from some form of dementia (8). According to *Older Americans 2000: Key Indicators of Well-Being* (9), in 1998 about 4% of adults aged 65 to 69 had moderate to severe memory impairment (a measure of low cognitive functioning), compared with about 36% of adults aged 85 or older. The prevalence of low cognitive functioning was found to be slightly less among women aged 85 and older than among men of the same ages (35% and 37%, respectively). An estimated 5% to 8% of people aged 65 and older have some form of dementia; this number doubles for every five years over age 65.

As many as seven million people in the United States suffer from some form of dementia. An estimated 40,000 individuals in West Virginia had Alzheimer's disease in 2000. By 2025, the state is expected to experience a 25% increase in number of persons with AD, to 50,000.

Alzheimer's disease alone affected approximately 4.5 million Americans in 2000 (10). Estimates of the annual number of new clinically diagnosed cases (incidence) of AD range from 250,000 to 360,000 (11,12). As the population ages, however, these numbers are expected to rise. Research presented in 2002 at the 8th International Conference on Alzheimer's Disease and Related Disorders (ICAD) and published in the August 2003 issue of the *Archives of Neurology* makes dire predictions about the future of AD in the United States (10). Evans et al., the study's authors, based their findings on data from the Chicago Health and Aging Project, which was supported by the National Institutes of Health. They project that by 2050 an estimated 13.2 million Americans will have AD if nothing is done to forestall or treat the disease. The table below shows these projections, in millions, by age group:

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**

The situation is even more serious among minorities. Research reported at the 9th ICAD held in 2004 suggested that minorities were underrepresented in the study by Evans et al. and thus will face an even greater problem if interventions to prevent and treat AD are not implemented. A University of Pennsylvania study found that AD symptoms first appeared at an average age of 67.6 in Latinos, compared with 73.1 among non-Latinos (13). In another study presented at the conference, researchers found much higher rates of AD among African-Americans than among whites (14). The study was conducted in South Carolina, one of only two states that keep an Alzheimer's registry. Among persons aged 55-64, the rate of AD was more than three times higher among blacks than whites; among persons aged 65 to 84 the rate was more than double and in persons over the age of 85, blacks were 1.5 times more likely to be diagnosed with AD.

Evans et al. expanded their study to include state-specific projections of AD prevalence through 2025 and published their results in *Neurology* in 2004. For West Virginia, their model produced an estimate of 40,000 affected individuals in 2000. By 2025, the state is expected to experience a 25% increase in number of persons with AD, to 50,000 (15).

A 1998 study by Brookmeyer et al. estimated the 1997 prevalence of AD at 2.3 million (1.09 to 4.58), a more conservative estimate than that derived from the Evans et al. model (12). Published in the *American Journal of Public Health* in 1998, the authors projected that the prevalence of Alzheimer's would quadruple by 2047, afflicting approximately 1 in 45 Americans at that time if steps were not taken to delay onset. According to their research, if interventions could be implemented that would delay the onset of AD by two years, there would be 2 million fewer cases in 2047. The delay of symptoms by just one year would result in 800,000 fewer cases.

COSTS OF DEMENTIA

The estimated economic costs of Alzheimer's disease in the United States total at least $100 billion annually; it is considered the third most expensive disease to treat (16). Per patient costs for nursing home care alone for persons with AD range from $42,000 to $70,000 a year (17). In addition, it is estimated by a University of Pennsylvania study that the cost to business approaches $61 billion (18). The study, *Alzheimer's Diseases: The Costs to U.S. Businesses in 2002*, breaks this figure down between health care for people with AD ($24.6 billion) and costs incurred by caregivers ($36.5 billion), which include absenteeism ($10 billion), productivity losses ($18 billion), and worker replacement costs ($6 billion).

As dementia, and AD in particular, is primarily an illness of the elderly, the costs to Medicare are tremendous. The number of Medicare beneficiaries with AD increased by 250% in the 1990s according to researchers at Duke University (19). Among African-Americans, the increase was a staggering 460%. Medicare costs for AD patients are nearly three times higher than the average for all beneficiaries; it is estimated that Medicare expenditures for AD will increase by 55% to $50 billion in less than 10 years, while the costs to Medicaid will increase 80%, to $33 billion. To quote Sheldon Goldberg, the president and CEO of the Alzheimer's Association, "Unless a prevention or cure is found soon, Alzheimer's disease will overwhelm our already stretched health-care system and bankrupt Medicare and Medicaid."

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The costs of treating AD increase with the severity of the disease. Leon et al. analyzed 1996 data and estimated (in 1996 dollars) the monthly costs of caring for a patient suffering from mild (early onset) AD to be $1,534, while the costs for someone with moderate AD was $2,054, and those for a patient with advanced AD was $3,011 (2). These costs have increased substantially since then, but indicate the increased care needed as AD progresses. More recently, 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 (19). 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.

While the costs of treating vascular dementia were not found to be significantly different than those for treating AD in a research project by the Institute for the Study of Aging, the subgroup of patients with arteriosclerotic dementia/multi-infarct dementia had costs that were significantly higher ($10,555/year) than those with AD (20).

RISK FACTORS FOR DEMENTIA

The greatest risk factor for Alzheimer's disease is **age**. While about 10% of people in the United States over the age of 65 have AD, it is estimated that nearly 50% of those over age 85 are at risk for developing the disease (21). **Women** are more likely than men to develop AD; this may be age-related, as women live longer than men.

Research has also shown that individuals with a **family history** of AD are more likely to have the disease themselves (21). People who have a specific version of the apoE gene (i.e., apoE 4), 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 (22). In 2000, three separate studies found that chromosome 10 might also have genes that increase a person's chances of developing late-onset AD (23). Early-onset AD is even more likely to run in families. Scientists have found that families with a history of early-onset AD have a mutation in selected genes on chromosomes 21, 14, and 1. Children who have one parent with the mutation have about a 50-50 chance of developing early-onset AD (24).

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 (25). 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 possible factor in the development of AD. The types of cells and compounds normally involved in inflammation have been found in AD plaques, leading some scientists to suggest that these aid in the development of the plaques that ultimately cause the neurons to die (25). A study that analyzed the medical records of World War II veterans linked **head injury** in early adulthood to AD in later life (26). The authors speculated that brain trauma can trigger a degenerative process that eventually results in the development of AD.

Down's syndrome, head injury, learning disabilities, and low educational achievement are all associated with a higher risk of developing Alzheimer's disease in later life.

The Alzheimer's Society reports that individuals with **Down's syndrome** (trisomy 21) have a higher incidence of developing AD in middle age (27). The prevalence of dementia in people with other **learning disabilities** is four times higher than that in the general population (27). **Low educational achievement** has been found to lead to an increased risk for AD in other studies (28).

Some researchers have been studying the associations between AD and exposure to **environmental toxins**. A study from Case Western Reserve University found that people working in jobs that involved high levels of lead exposure were 3.4 times more likely to develop AD (29). Other studies have examined the roles of aluminum and mercury in the development of AD, but results have been mixed. Scientists at the University of Calgary Faculty of Medicine published findings in 2001 showing that exposure to mercury in animal subjects caused the formation of neurofibrillary tangles, one of the markers for AD (30). An earlier Swiss study linked mercury exposure to amyloid plaques in animal tests (31). Other studies have found an association between brain degeneration in animals and the mercury in dental amalgams (32), but a 1999 study at the University of Kentucky found no such link in human subjects (33).

Cerebral infarctions (strokes) are associated with vascular dementia, especially in the elderly, and impaired cognitive function. A recent study published in *Neurology* found a twofold increase in the risk of vascular dementia following a cerebral infarction (34). 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 Alzheimer's disease as well (35). 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.

Alzheimer's disease is increasingly viewed as having a vascular basis and subject to the same risk factors as cardiovascular disease: smoking, high cholesterol, hypertension, physical inactivity, diets deficient in fruits and vegetables, and diabetes. West Virginia adults report **significantly higher-than-average** rates of all of these.

The connection between Alzheimer's disease 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, such as **smoking, high cholesterol, hypertension, physical inactivity, 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.

Table 1 below contains 2003 West Virginia and United States prevalence rates for these risk factors. The state's rates of all six risk factors were **statistically significantly higher** than the national rates.

Table 1. Prevalence (%) of Selected Risk Factors* Among Adults (18 and Older) West Virginia and United States (Median) 2003 Behavioral Risk Factor Surveillance System

Risk Factor	Total		Male		Female	
	WV	US	WV	US	WV	US
Cigarette Smoking[1]	27.3	22.0	27.6	24.7	27.1	20.2
High Cholesterol[2]	38.1	33.1	33.8	33.8	41.7	32.1
Hypertension[3]	33.6	24.8	35.0	25.0	32.3	24.9
Physical Inactivity[4]	28.0	23.1	24.9	20.8	30.9	24.9
Poor Nutrition[5]	81.3	77.4	84.9	82.3	77.9	73.0
Diabetes[6]	9.8	7.2	8.7	7.3	10.8	7.0

*Factors that are currently viewed as potential risks for developing dementia.
Source: http://www.cdc.gov/brfss/

[1] Currently smokes cigarettes.
[2] Has been told by a health professional that blood cholesterol level is high.
[3] Has been told by a health professional that he/she has high blood pressure.
[4] Reported no physical activity during the month prior to the interview.
[5] Consumes fewer than five fruits and vegetables per day.
[6] Has been told by a health professional that he/she has diabetes.

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 (36). Mild cognitive impairment before surgery was a predictor of more severe long-term cognitive impairment following surgery. The use of heart-lung machines has been suggested as a cause, through the release of embolic material that can enter the cerebral vessels during surgery (37). The Duke researchers suggest a different theory: The heart-lung machine reduces blood flow throughout the body during surgery, resulting in less blood flow to the intestines, starting a process whereby bacteria enter the bloodstream, causing inflammation in the brain (38). Bypass surgeries performed without a heart-lung machine and other surgeries such hip replacements can also result in increased dementia, however, causing some researchers to focus instead on the role of anesthesia (39). Research continues to be performed on factors of surgical procedures that may impact long-term cognitive function.

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 slow its progression.

"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 carried out by researchers at the University of Kentucky examined the autobiographies of nearly 100 nuns written as young women (40). 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 (41). Their findings, published in the *New England Journal of Medicine* in June 2003, 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 Alzheimer's disease and vascular dementia. In addition, the more frequent the activity, the lower the risk.

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 protects them from dementia.

Occupational history may also play a role in the development of dementia. Researchers at Case Western Reserve University School of Medicine studied the link between having a mentally demanding occupation and the later development of AD (42). They found that people in mentally challenging occupations in their thirties, forties,

and fifties were less likely to develop AD. Scientists speculate that mentally engaged people build up a "brain reserve" that protects them from dementia. 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 (43).

Cardiovascular Risk Factors. According to Marilyn Albert, a Johns Hopkins University researcher with the Alzheimer's Association, "If you do things that are good for your heart, they'll be good for your brain" (44). Scientists are finding evidence that being physically active, having good cholesterol, maintaining a healthy weight, and controlling blood pressure can lower the risk of developing dementia as well as heart disease.

Two separate studies published in the *Journal of the American Medical Association* in September 2004 found an association between physical activity and better cognitive function in older adults. 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 (45). In the Honolulu-Asia Aging Study, 2,257 physically capable men aged 71 to 93 were assessed over eight years to determine if walking is associated with the risk of developing dementia. Abbott et al. found that the men who walked the least (<0.25 mile/day) had a 1.8-fold excess risk of developing dementia as compared with men who walked more than two miles per day (46). Men who walked from 0.25 to one mile per day were 1.7 times more likely than the more active men to develop dementia.

Using data from 18,766 women aged 70 to 81 years who participated in the Nurses' Health Study, Harvard researchers Weuve et al. also found a positive association between physical activity and better cognitive performance. Women who walked at least 1.5 hours per week had less cognitive decline than those who walked less than 40 minutes per week (46).

Research has found an association between physical activity and improved cognitive function. Exercise can prompt the development of new brain cells while also triggering the release of a substance that can protect the cells.

Three studies presented at the 9th International Conference on Alzheimer's Disease and Related Disorders held in July 2004 examined other known cardiovascular risk factors and their links to dementia. 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 (47). Women whose HDL levels were in the 60 to 75 mg/dL range decreased their risk of dementia by almost 50%.

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 all hypertension medications; however, the risk reduction varied by type of medication. While use of any blood pressure medication lowered risk by 36%, diuretics were associated with an overall 40% risk reduction and users of a class of diuretic called potassium-sparing experienced a 75% reduction in Alzheimer's risk (48).

Another finding, presented by University of Washington researcher Suzanne Craft, concerned Avandia, an oral diabetes medication, and memory. Avandia was found to improve memory and thinking ability in people with mild AD (48). Craft theorizes that Avandia works because it reduces a person's insulin resistance, which in turn lowers levels of beta-amyloid protein in the blood, the protein found in plaques in the brains of AD patients.

You Are What You Eat. Diet is being increasingly studied in terms of how what we eat influences our risk of developing dementia. A Finnish study presented at the 9th ICAD linked obesity with an increased risk of developing dementia. Dr. Mila Kivipelto's study included 1,449 Finns whose BMI was calculated when they were in middle age and who were then reexamined an average of 21 years later (49). She found that the risk of any dementia, but AD in particular, doubled with a BMI of 30 or greater (obese).

You are what you eat: Studies have shown that high fat and high calorie diets are associated with a greater risk of developing Alzheimer's disease, while fish consumption is associated with a lower risk.

One of the first studies to link specific foods and AD was conducted by researcher William Grant, who analyzed data from 18 different studies involving populations of people aged 65 and older in 11 countries. Dr. Grant's study, "Dietary Links to Alzheimer's Disease," concluded that high fat and high calorie diets have a direct association with high AD prevalence rates (50). He also found that fish consumption reduced the incidence of AD in North America and Europe. 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 (51). Those people who ate large quantities of saturated (animal-based) fats, on the other hand, had double the risk of AD compared with people who ate small amounts.

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 (52). 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." 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 (51).

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 ten 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 (53). 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 Alzheimer's (54). 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 (55). 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 fourth study, of 980 elderly Medicare patients in New York, found no evidence of a decreased risk of AD with any form of antioxidant intake (56).

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 (57). 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.

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. Szekely et al. conducted a meta-analysis of published studies on exposure to nonaspirin NSAIDs and the risk of AD. Eleven studies met the criteria for inclusion. In all, both prospective and nonprospective, NSAID exposure was associated with a decreased risk of developing AD (58). The duration of NSAID use was found to be important in the Rotterdam study (59). No statistically significant findings resulted from use of less than 24 months, while taking an NSAID for 24 months or longer resulted in a likelihood of developing AD that was only 20% of that

for non-users. Since NSAIDs can cause gastrointestinal bleeding, safe dosage and duration have yet to be determined.

Hormone Use. Contradictory evidence has been found in studies on the effect of the hormone estrogen on AD development in older women. Several pre-2000 studies found a positive association between taking estrogen supplements and a decreased risk of AD (60). Data from the Women's Health Initiative Memory Study found just the opposite effect, however, i.e., an actual increase in the risk of dementia among postmenopausal-aged women among those participants taking estrogen plus progestin (61,62). More research is necessary to determine how estrogen therapy affects AD.

Scientists have recently turned their attention to the link between testosterone levels and AD risk. Laboratory models have shown that testosterone reduces the formation of both beta-amyloid plaques and tau protein (63). Moffat et al. studied data on 574 men participating in the Baltimore Longitudinal Study for a mean of 19.1 years and found that free testosterone concentrations (but not testosterone bound to sex hormone binding globulin) were lower in men who developed AD (64). Additional research is required to determine whether free testosterone levels offer protection against AD in older men.

Lithium. A small study presented at the 9th ICAD linked lithium, a common treatment for bipolar disorder, with a decreased risk of AD. Nunes et al., from the University of Sao Paolo, Brazil, found that within their study population of 74 elderly individuals with bipolar disorder, 4% of those who had been taking lithium had AD, compared with 21% of patients not taking the drug (65). A Japanese team of scientists reported at the same conference that they had found decreased tau protein tangles in the brains of mice genetically altered to have AD that had been treated with lithium (65). Lithium also stopped the development of plaques in those mice. Research is ongoing to determine the mechanism by which the drug prevents or destroys the hallmark plaques and tangles of AD.

Vaccine. Several research projects are currently under way to develop a vaccine to treat and perhaps prevent Alzheimer's disease. 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 (66). When the brain of a woman who had taken the vaccine and died after a fall was examined, scientists found fewer plaques but also T cells, which are not normally found in the brain, signaling that an overreaction of the immune system caused the inflammation.

Several research projects are currently under way to develop a vaccine to treat and perhaps prevent Alzheimer's disease. Most of these involve using the body's own immune system to produce antibodies to attack and clear the beta-amyloid plaques.

Other researchers are now pursuing the same general immune-

system strategy using different formulations. A paper published in October 2004 in the *Journal of Alzheimer's Disease* discusses a new oral vaccine treatment developed by researchers from the National Institute for Longevity Studies (Japan) and the Harvard Institute of Medicine (67). According to lead author Hideo Hara, MD, "This new oral vaccine does not induce strong T cell immune reactions, and hence could reduce the side effect of such meningoencephalitis . . . This new therapy seems to be effective for prevention and treatment of Alzheimer's disease." Human trials had not been initiated at the time of this report's publication.

DIAGNOSIS OF DEMENTIA

As treatments for AD and vascular dementia are 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. Brain scans have become available recently that allow doctors to distinguish between vascular dementias and AD. In 2003, researchers at the San Francisco VA Medical Center used magnetic resonance imaging (MRI) along with magnetic resonance spectroscopy to correctly identify 90% of patients who had vascular dementia (68). Vascular dementia, frontotemporal dementia, and dementia with Lewy bodies are all a result of degenerative vascular brain disease.

Researchers are also working on developing neuroimaging methods that can assist in the early detection of AD. MRI scans, computed tomography (CT), single photon emission computed tomography (SPECT), and positron emission tomography (PET) are all being studied as aids in the diagnosis of AD. Neuroimaging techniques are invaluable in researching brain changes that occur in the different stages of AD; however, they represent only one step in diagnosing AD, that of ruling out a vascular cause for a patient's dementia. As new medications become available for AD, neuroimaging will also allow researchers to determine their efficacy in eliminating plaques and tangles or at least slowing the progression of the disease.

To diagnose AD, doctors usually rely on several evaluations. 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 comes only with an examination of the brain tissue itself.

TREATMENT OF 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. The majority of drugs being used currently to treat AD 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. By early 2004, the FDA had approved four cholinesterase inhibitors to treat mild to moderate AD symptoms: donepezil (Aricept), rivastigmine (Exelon), galantamine (Reminyl), and tacrine (Cognex).[7] Donepezil has also been shown to be effective in treating vascular dementia (69,70).

Another class of drugs approved to treat AD is that of NMDA receptor agonists, which regulate the activity of glutamate, another brain chemical involved in memory function. As of mid-2004, only one drug in this class, memantine (Namenda), had been approved to treat AD, but several others were in clinical trials (71). Memantine may delay loss of daily function in patients with moderate to severe AD.

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.

A third class of drugs being tested are anti-amyloid drugs such as the vaccines discussed above. These drugs prevent the formation of the beta-amyloid plaques by inhibiting the enzyme gamma secretase. This prevents the strings of beta-amyloid from clumping together. One anti-amyloid drug called Alzhemed is currently undergoing efficacy trials (72).

The 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. A 2004 French study presented findings that statin drugs used to lower cholesterol also had therapeutic benefit for AD. Statin treatment was associated with a slower rate of cognitive decline, perhaps due to a mechanism independent of the cholesterol-lowering action (73).

[7] Currently, Cognex is rarely used because of serious side effects.

Antiplatelet agents such as aspirin, clopidogrel (Plavix), and extended-release dipyridamole (Aggrenox) that prevent clotting and hemorheologic agents such as pentoxifylline (Trental) that lower blood viscosity are frequently prescribed. Antidepressant drugs may be used to treat the depression that often accompanies vascular dementia.

In addition to conventional drug therapies, new research presented at the American Heart Association's Second Asia Pacific Scientific Forum in 2003 suggests that a Chinese herb called gastrodine could improve memory, orientation, and language in patients with mild to moderate vascular dementia (74).

DEMENTIA DIAGNOSES IN HOSPITAL RECORDS

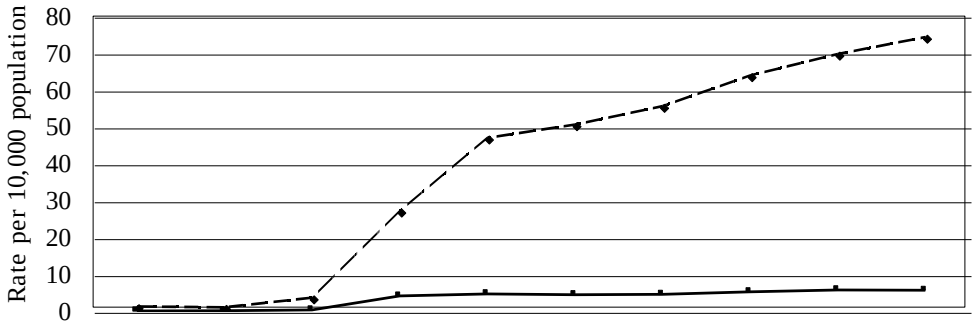
Hospital discharge data provide an additional source of information on the prevalence of disease and the burden on the state. Data from the West Virginia Health Care Authority (WVHCA) were used to determine the rate of hospitalizations that included any diagnosis of dementia. The WVHCA collects inpatient 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).

1992-2001 Hospitalizations. The overall rate of hospital discharges among state residents with a principal or secondary diagnosis of dementia from 1992 to 2001 ranged from a low of 1.1 per 10,000 discharges in 1993 to a high of 74.3 in 2001. The total charges billed for hospitalizations with a principal diagnosis of dementia ranged from $136,000 in 1992 to $7,750,000 in 2000. The dramatic increases in diagnoses and charges related to dementia (shown in Figures 1 and 2) reflect both an increase in the state's older population and an enhanced awareness of the condition, especially AD.

2001 Hospitalizations. Approximately 5% of all discharges both nationally and statewide in 2001 had dementia as either a principal or secondary diagnosis. In West Virginia, 13,390 of 252,983 resident discharges, or 5.3%, included a dementia diagnosis; nationally, about 1,651,000 of 32,653,000 discharges, or 5.1%, had such a diagnosis.

West Virginia's rate (per 10,000 population) of hospitalizations with a diagnosis of dementia in 2001 was 74.3, compared with a rate of 58.2 for the United States, a difference of 28%. (Part of this difference is due to the fact that West Virginia had a rate of total discharges in 2001 that was 22% higher than that for the nation as a whole.) When looking just at AD, the state rate was 68% higher than the national rate. As Table 2 shows, the state had higher rates of dementia diagnoses among both men and women and among patients aged 65 and older. Only among patients aged 45-64 was the state rate equal to or lower than the national rate.

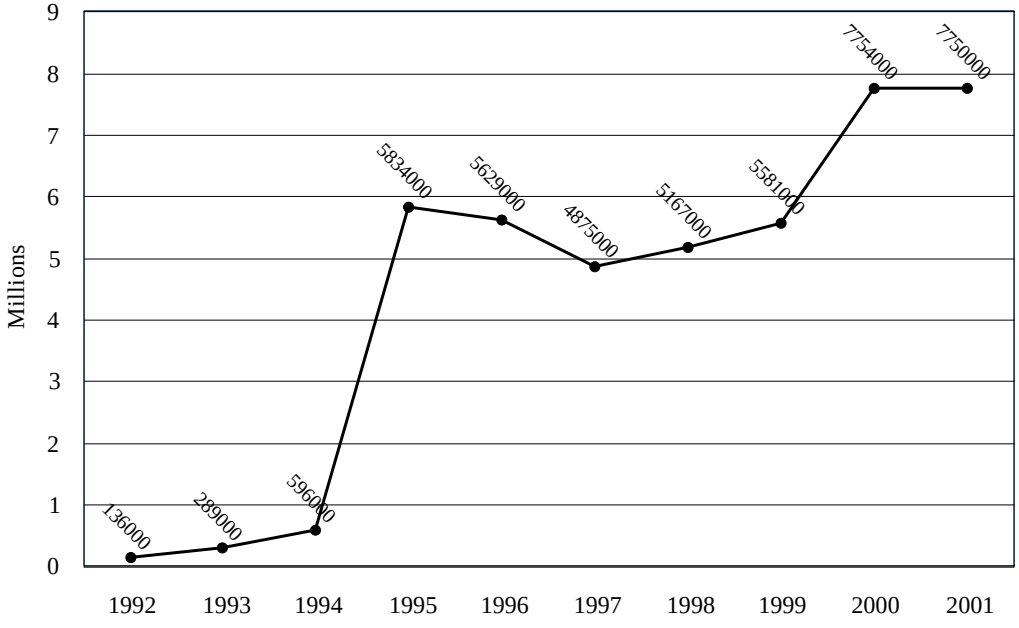
Figure 1. Rate of Inpatient Hospital Discharges Having a Principal or Secondary Diagnosis of Dementia
West Virginia Resident Hospitalizations, 1992-2001



	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001
Principal	0.1	0.2	0.4	4.2	4.7	4.5	4.6	5.3	5.8	5.7
Any-Liste	1.3	1.1	3.7	27.2	47	50.6	55.6	63.9	69.7	74.3

* Dementia defined as ICD-9 codes 290.XX, 294.1 and 294.8, and 331.0
Rates calculated using 2000 census population of 1,801,641.

Figure 2. Estimated Charges for Hospital Discharges
Having a Principal Diagnosis of Dementia*
West Virginia Residents, 1992-2001



*Dementia defined as ICD-9 codes 290.XX, 294.1 and 294.8, and 331.0

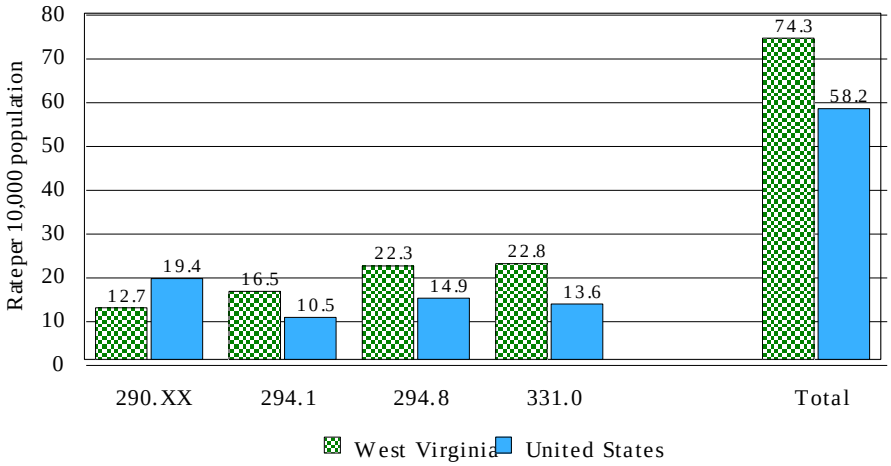
Table 2. Rate (per 10,000 Population) of Resident Inpatient Hospital Discharge Records Having a Principal or Secondary Diagnosis of Alzheimer's Disease or Other Dementia, by Gender and Age
West Virginia and United States, 2001

	West Virginia			United States		
	Alzheimer's	Other*	Total	Alzheimer's	Other*	Total
Total	22.8	51.6	74.3	13.6	44.5	58.2
Gender						
Male	14.5	33.8	48.3	12.6	31.1	43.7
Female	30.6	68.3	98.9	20.8	55.9	76.7
Age						
45-64	1.2	6.0	7.2	1.2	8.5	9.8
65+	146.6	326.0	472.7	107.4	342.0	449.4

*Senile, presenile, and other organic psychotic conditions, including arteriosclerotic dementia
Rates calculated using 2000 census populations.

When broken out by most frequently diagnosed types of irreversible dementia, illustrated in Figure 3, the overall state rate of senile and presenile organic psychotic conditions, including arteriosclerotic dementia, is shown to be lower than the U.S. rate. Dementia resulting from other chronic organic psychotic conditions and AD, however, is diagnosed more frequently among West Virginia residents than in the United States as a whole.

Figure 3. Rate of Inpatient Hospital Discharge Records Having a Principal or Secondary Diagnosis of Dementia, by Type of Dementia
West Virginia (Residents) and United States, 2001



290.XX = Senile and presenile organic psychotic conditions, including arteriosclerotic dementia
294.1 and 294.8 = Chronic organic psychotic conditions not classified in 290.XX
331.0 = Alzheimer's disease

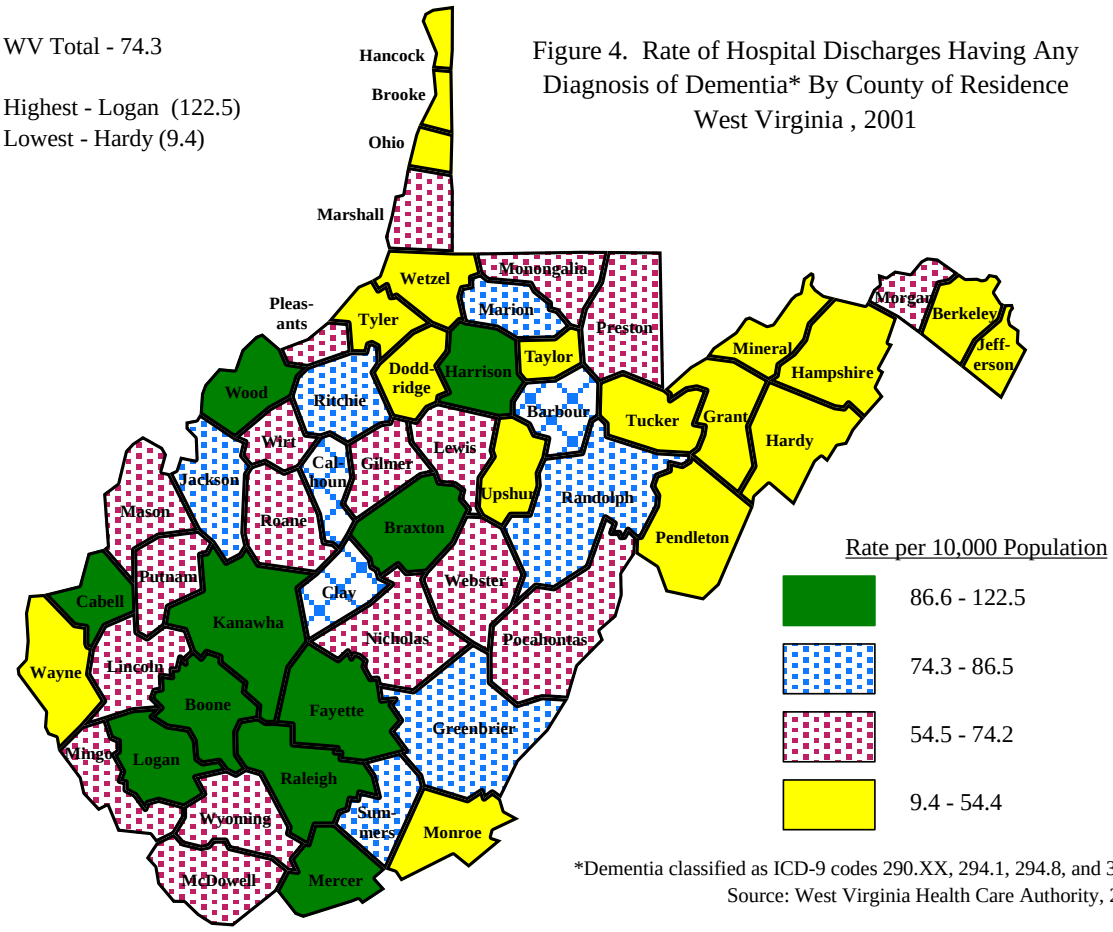
2001 Hospitalization Charges. In 2001, approximately $7,750,000 was billed for hospitalizations of West Virginia residents with a principal diagnosis of dementia, $3.3 million for AD and $4.4 million for other dementias. Approximately 90% of these charges were billed to Medicare, as would be expected, with the remaining 10% divided somewhat evenly among Medicaid, PEIA, and other payers.

County-Specific Rates. The rate of hospital discharges having a principal or secondary diagnosis of dementia in 2001 ranged from a high of 122.5 per 10,000 discharges among Logan County residents to a low of 9.4 among Hardy County residents. As shown in Figure 4, the highest rates of dementia among patients were reported in the southern counties of West Virginia, while the lowest rates were concentrated in the eastern part of the state. Individual county rates and ranks are found in Appendix A.

WV Total - 74.3

Highest - Logan (122.5)
Lowest - Hardy (9.4)

Figure 4. Rate of Hospital Discharges Having Any Diagnosis of Dementia* By County of Residence West Virginia , 2001

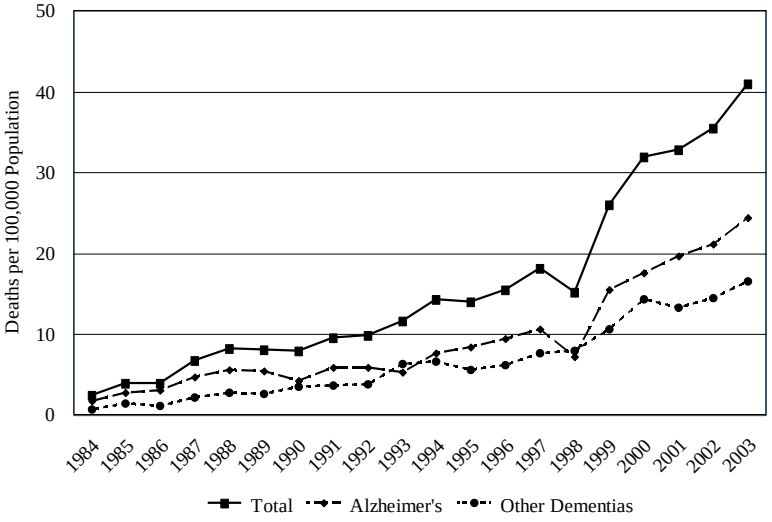


*Dementia classified as ICD-9 codes 290.XX, 294.1, 294.8, and 331.0
Source: West Virginia Health Care Authority, 2004

DEMENTIA MORTALITY

Most people who suffer from dementia do not die from the disease itself but from a secondary condition such as pneumonia or complications from a fall. Even so, the rate of deaths with Alzheimer's disease or other dementia listed as the underlying, or primary, cause of death is increasing. Figure 5 shows the trends in mortality from AD, other dementias, and total dementias from 1984 through 2003 (actual rates are found in Appendix B). Coding changes in 1999[8] likely accounted for the marked increase in rates in that year; however, both pre-1999 and post-1999 rates show a consistent upward trend.

Figure 5. Mortality Rates for Alzheimer's Disease and Other Dementias
West Virginia Residents, 1984-2003



This increase can be attributed to several factors, including more awareness of AD and other dementias, earlier diagnosis of the illnesses, and an aging population. AD first appeared in the 10 leading causes of death in West Virginia in 2000; nationally this occurred in 1999. By 2002, AD was the eighth leading cause of death in both the state and the nation.

Figure 6 illustrates the upward trend in dementia mortality by gender over the same 20-year period. While the increase is apparent among both sexes, with similar rates until 1999, women have been more likely to die from dementia than men since 2000. (Individual rates are found in Appendix B, as well as a breakdown between Alzheimer's disease and other dementias.)

[8] A new cause-of-death classification, International Classification of Disease, Revision 10 (ICD-10), was introduced in 1999, superceding ICD, Revision 9 codes that had been in use since 1979. The difference in coding resulted in slightly higher rates for some causes.

Figure 6. Mortality Rates* for Dementia (Alzheimer's Disease and Other Demei
By Gender, West Virginia Residents, 1984-2003

*Rates are age-adjusted to the U.S. standard million.

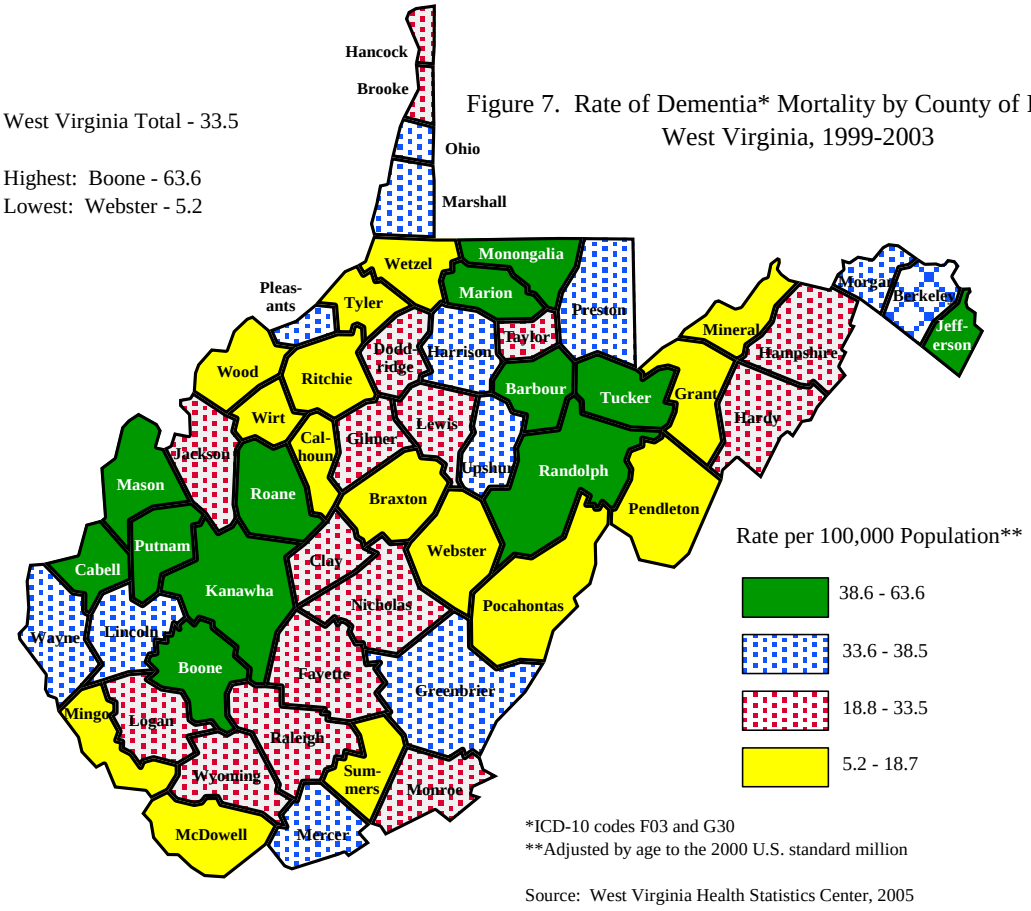
County-Specific Mortality Rates. Data on dementia mortality were aggregated for the years 1999-2003 in order to examine deaths on the county level and are presented in Figure 7 on the next page. Mortality rates for dementia ranged from a high of 63.6 deaths per 100,000 population in Boone County to a low of 5.2 in Webster County. The highest rates are found in the west-central and northern sections of the state. Individual county rates and ranks are found in Appendix C.

State and National Dementia Mortality Rates Among Older Adults. At the time this report was prepared, the National Center for Health Statistics (NCHS) had published (on-line) mortality rates from 1982 through 2001 for selected causes, including Alzheimer's disease, among people aged 65 and older of both sexes and all races. These data are presented with comparable West Virginia rates in Figure 8. As can be seen, the overall age-specific rates were similar in both the state and the nation throughout the 20-year time period.

West Virginia Total - 33.5

Highest: Boone - 63.6
Lowest: Webster - 5.2

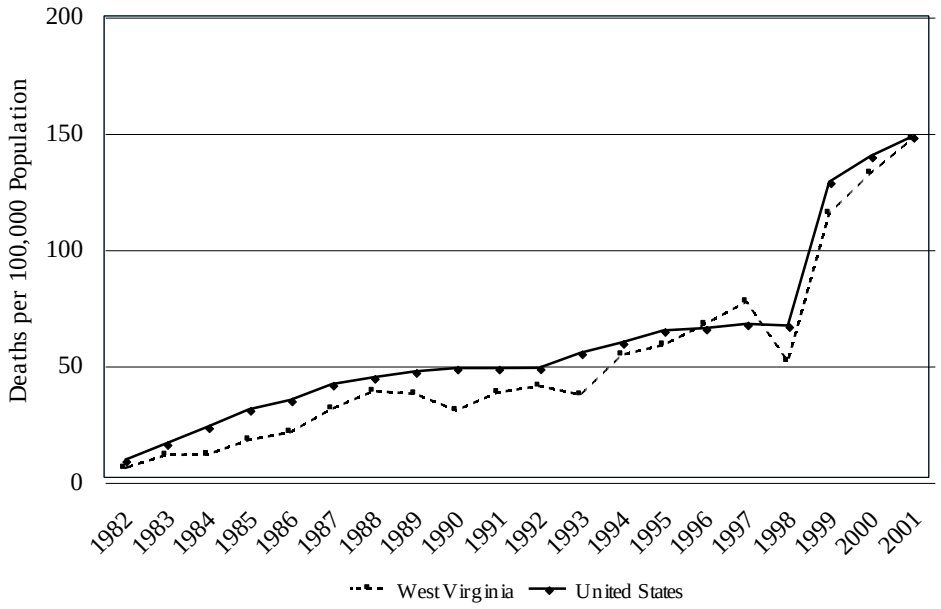
Figure 7. Rate of Dementia* Mortality by County of Residence
West Virginia, 1999-2003



*ICD-10 codes F03 and G30
**Adjusted by age to the 2000 U.S. standard million

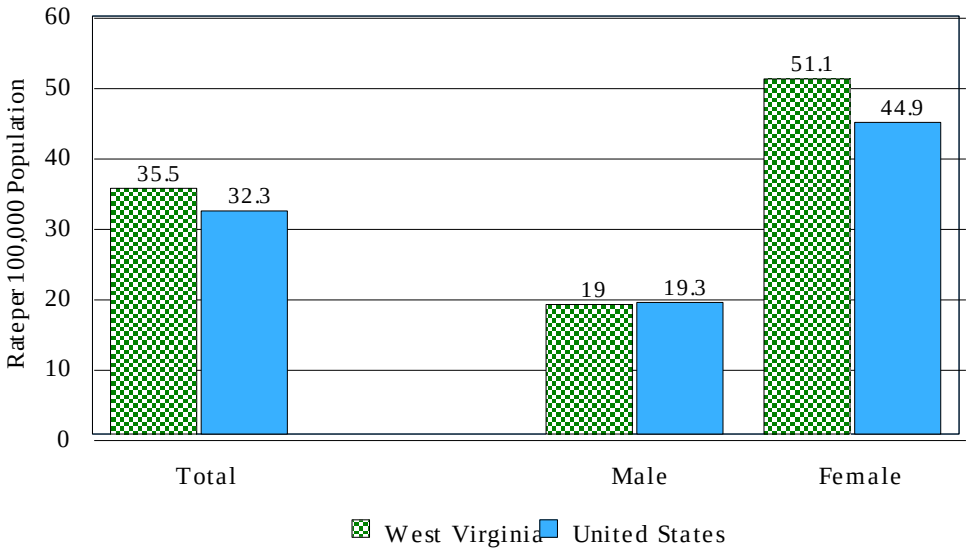
Source: West Virginia Health Statistics Center, 2005

Figure 8. Mortality Rates from Alzheimer's Disease Among Persons Aged 65+
West Virginia and United States, 1982-2001



Multiple-Cause-of-Death Data. The National Center for Health Statistics (NCHS) compiles and collects data on all deaths in the United States according to ICD-10. The information collected by NCHS is released on annual multiple-cause-of-death tapes that include the following: decedent's age, sex, race, and state of residence; the underlying cause of death, and contributing causes of death (up to 19 additional causes). This analysis examines multiple-cause-of-death data related to dementia for West Virginia and the United States for 2001. Overall, as shown in Figure 9, the mortality rate for dementia as the underlying cause was nearly 10% higher in West Virginia than in the United States as a whole. While virtually no difference was seen among men, the rate among state women was 14% higher than their counterparts elsewhere. Overall mortality rates for dementia as an any-listed (underlying or contributing) cause were 38% higher in the state than in the nation, with higher rates among both state men and women (Figure 10).

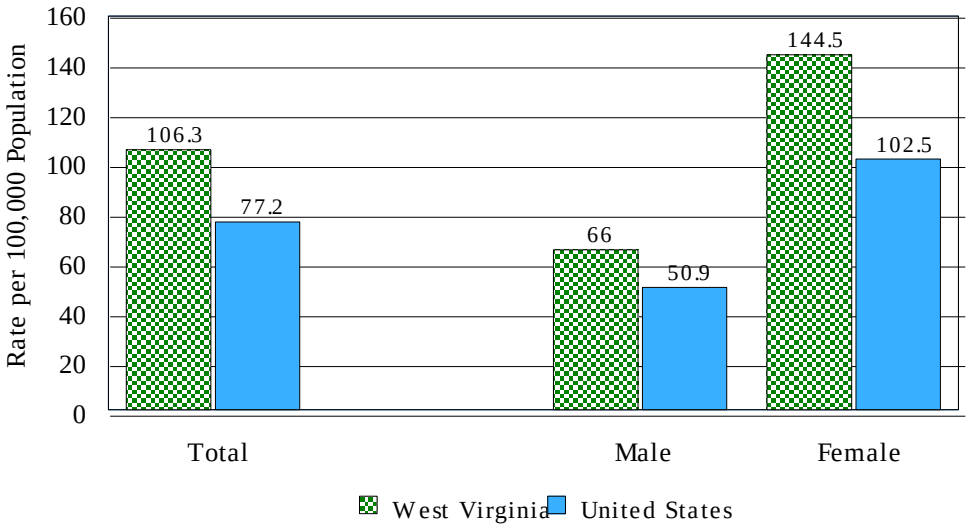
Figure 9. Mortality Rates from Dementia* as Underlying Cause of Death
West Virginia and United States
2001 Mulitple Cause of Death File



*Dementia is classified as ICD-10 codes F03 (unspecified presenile and senile dementias) and G30 (Alzheimer's disease).

While higher overall rates of dementia mortality are not unexpected in the state due to West Virginia's older population, it would be expected that these differences would decrease with age-specific rates if age were the only factor involved. As Table 4 shows, these differences persist in West Virginia among women aged 65-84 with dementia diagnosed as the underlying cause of death and among both sexes with dementia diagnosed as an any-listed cause.

Figure 10. Mortality Rates from Dementia* as Any-Listed Cause of Death
West Virginia and United States
2001 Mulitple Cause of Death File



*Dementia is classified as ICD-10 codes F03 (unspecified presenile and senile dementias) and G30 (Alzheimer's disease)

Table 4. Mortality Rates (per 100,000 Population) for Dementia* by Gender and Age West Virginia and United States, 2001 Multiple Cause of Death File

	Underlying Cause		Any-Listed Cause	
	West Virginia	United States	West Virginia	United States
Male				
0-64	0.4	0.4	1.0	1.2
65-74	27.1	29.1	76.8	80.8
75-84	177.2	221.4	732.8	596.1
85+	901.4	1055.0	2794.4	2691.4
Total	**19.0**	**19.3**	**66.0**	**50.9**
Female				
0-64	0.3	0.4	1.0	1.0
65-74	32.9	28.8	90.2	67.3
75-84	227.3	245.0	697.0	569.4
85+	1357.8	1414.7	3698.0	3199.7
Total	**51.1**	**44.9**	**144.5**	**102.5**
Both Sexes				
0-64	0.3	0.4	1.0	1.1
65-74	30.3	29.0	84.2	73.4
75-84	208.0	235.7	710.8	580.0
85+	1230.4	1310.6	3445.7	3052.6
Total	**35.5**	**32.3**	**106.3**	**77.2**

*Dementia is classified as ICD-10 codes F03 (unspecified presenile and senile dementias) and G30 (Alzheimer's disease). Rates were calculated using the 2000 census populations.

DEMENTIA RESEARCH

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 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 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**" (75). The challenge now is to find the key to keeping our brains healthy throughout our life spans.

Appendix A. Rate of Inpatient Hospital Discharge Records Having an Any-Listed Diagnosis of Dementia by Patient's County of Residence, 2001				
	Estimated 2001 Population	Number of Discharges	Rate per 10,000 Population	Rank
Barbour	15,438	116	75.1	19
Berkeley	78,680	234	29.7	50
Boone	25,502	226	88.6	10
Braxton	14,763	147	99.6	7
Brooke	25,196	132	52.4	40
Cabell	95,850	949	99.0	8
Calhoun	7,416	58	78.2	15
Clay	10,288	86	83.6	12
Doddridge	7,449	26	34.9	48
Fayette	47,227	490	103.8	5
Gilmer	7,110	52	73.1	20
Grant	11,344	13	11.5	54
Greenbrier	34,429	267	77.6	16
Hampshire	20,660	38	18.4	51
Hancock	32,289	174	53.9	39
Hardy	12,802	12	9.4	55
Harrison	68,024	695	102.2	6
Jackson	28,040	217	77.4	17
Jefferson	43,411	140	32.2	49
Kanawha	197,671	2,059	104.2	4
Lewis	16,917	106	62.7	30
Lincoln	22,171	159	71.7	23
Logan	36,888	452	122.5	1
McDowell	26,549	178	67.0	27
Marion	56,266	427	75.9	18
Marshall	35,294	222	62.9	29
Mason	26,076	171	65.6	28
Mercer	61,991	723	116.6	2
Mineral	27,023	46	17.0	52
Mingo	27,554	192	69.7	24
Monongalia	82,715	480	58.0	36
Monroe	13,247	57	43.0	45
Morgan	15,223	85	55.8	37
Nicholas	26,310	190	72.2	22
Ohio	46,663	199	42.6	46
Pendleton	8,079	13	16.1	53
Pleasants	7,593	45	59.3	33
Pocahontas	8,937	62	69.4	25
Preston	29,290	172	58.7	35
Putnam	51,730	305	59.0	34
Raleigh	78,503	835	106.4	3
Randolph	28,262	228	80.7	14
Ritchie	10,341	84	81.2	13
Roane	15,458	95	61.5	31
Summers	14,214	123	86.5	11
Taylor	16,104	71	44.1	44
Tucker	7,215	28	38.8	47
Tyler	9,523	43	45.2	42
Upshur	23,349	127	54.4	38
Wayne	42,768	212	49.6	41
Webster	9,680	58	59.9	32
Wetzel	17,313	77	44.5	43
Wirt	5,890	43	73.0	21
Wood	87,711	781	89.0	9
Wyoming	25,205	170	67.4	26
WV Total	1,801,641	13,390	74.3	

Appendix B. Mortality Rates* for Alzheimer's Disease, Other Dementias, and Total Dementias, by Gender West Virginia Residents, 1984-2003

Year	Alzheimer's Disease			Other Dementias			Total		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
1984	2.2	1.5	1.7	0.3	0.9	0.7	2.5	2.4	2.5
1985	3.0	2.5	2.7	1.6	1.3	1.4	4.5	3.8	4.0
1986	2.8	3.1	3.0	0.9	1.1	1.1	3.8	4.1	4.0
1987	5.6	4.2	4.7	2.2	2.0	2.1	7.8	6.3	6.8
1988	7.0	5.3	5.9	2.3	2.5	2.4	9.3	7.8	8.3
1989	5.2	5.4	5.4	2.9	2.6	2.6	8.1	8.0	8.1
1990	5.3	3.8	4.3	2.8	3.9	3.5	8.1	7.8	7.9
1991	5.5	6.0	5.9	3.1	3.8	3.6	8.6	9.8	9.5
1992	5.9	5.9	5.9	3.8	3.8	3.8	9.7	9.8	9.8
1993	6.6	4.7	5.3	5.6	6.4	6.3	12.2	11.2	11.6
1994	7.6	7.6	7.7	7.2	6.2	6.6	14.8	13.8	14.3
1995	9.8	7.8	8.4	4.2	6.3	5.6	14.0	14.0	14.0
1996	8.6	9.4	9.4	5.4	6.3	6.1	14.1	15.8	15.5
1997	9.3	11.4	10.6	8.0	7.4	7.6	17.3	18.7	18.2
1998	7.1	7.2	7.2	7.1	8.3	8.0	14.2	15.6	15.2
1999**	14.6	15.9	15.5	9.9	10.8	10.6	24.5	26.7	26.1
2000	15.2	18.6	17.6	12.1	15.3	14.3	27.4	33.9	31.9
2001	15.5	21.6	19.7	11.4	14.0	13.3	26.9	35.6	32.9
2002	15.8	23.5	21.1	12.4	15.7	14.5	28.2	39.1	35.6
2003	20.4	26.3	24.4	14.5	17.4	16.6	34.9	43.7	41.0

*Rates are deaths per 100,000 population, age-adjusted to the 2000 U.S. standard million.
**In 1999, ICD-10 replaced ICD-9 in mortality coding.

Appendix C. Age-Adjusted (to 2000 U.S. Standard Million) Rate of Dementia Mortality by County of Residence, West Virginia, 1999-2003 (Aggregated Data)			
	Number of Deaths	Rate per 100,000 Population	Rank
Barbour	50	49.8	4
Berkeley	101	37.3	16
Boone	79	63.6	1
Braxton	17	17.2	46
Brooke	38	22.0	35
Cabell	297	50.6	3
Calhoun	9	17.9	42
Clay	16	31.2	26
Doddridge	12	30.5	28
Fayette	94	30.5	29
Gilmer	10	21.0	36
Grant	6	8.8	54
Greenbrier	84	34.4	21
Hampshire	20	18.9	39
Hancock	40	18.8	40
Hardy	17	25.3	32
Harrison	157	33.7	24
Jackson	48	31.8	25
Jefferson	86	53.1	2
Kanawha	555	44.1	8
Lewis	25	22.4	34
Lincoln	39	38.5	13
Logan	41	22.8	33
McDowell	27	16.3	48
Marion	166	39.4	11
Marshall	80	38.5	14
Mason	61	45.0	7
Mercer	149	35.8	20
Mineral	24	15.7	49
Mingo	20	17.7	44
Monongalia	170	49.0	6
Monroe	22	30.7	27
Morgan	30	36.5	18
Nicholas	38	26.6	31
Ohio	128	35.9	19
Pendleton	11	18.7	41
Pleasants	16	37.6	15
Pocahontas	8	12.0	52
Preston	56	34.2	22
Putnam	84	41.9	9
Raleigh	96	20.9	37
Randolph	88	49.1	5
Ritchie	8	12.8	50
Roane	35	40.7	10
Summers	19	16.9	47
Taylor	20	19.8	38
Tucker	20	38.6	12
Tyler	6	10.1	53
Upshur	56	37.0	17
Wayne	70	34.1	23
Webster	3	5.2	55
Wetzel	14	12.8	51
Wirt	5	17.4	45
Wood	95	17.7	43
Wyoming	29	26.7	30
WV Total	3,495	33.5	

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