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Thesis: Diagnosis and Treatment of Alzheimer's Disease: Current Challenges

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Thesis:

Diagnosis and Treatment of Alzheimer's Disease: Current Challenges

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Overview of Alzheimer's Disease

Alzheimer's disease (AD), the most common form of dementia, is a degenerative disorder of the brain that leads to memory loss¹. AD affects 5.3 million Americans and is the seventh leading cause of death in the United States. There are two main forms of the disease. Familial AD affects people younger than 65, accounting for nearly 500,000 AD cases in the United States alone¹. The remainder of AD cases occur in adults aged 65 and older and is classified as sporadic AD. The prevalence of AD varies among many different factors, including age, co-morbidities, genetics, and education level. There is no way to definitively diagnose AD without performing an autopsy. There is no cure for AD, however promising research and development for early detection and treatment is underway.

History

Alzheimer's disease was discovered in 1906 by Alois Alzheimer, a German neurologist and psychiatrist². The disease was initially observed in a 51-year-old woman named Auguste D. Her family brought her to Dr. Alzheimer in 1901 after noticing changes in her personality and behavior. The family reported problems with memory, difficulty speaking, and impaired comprehension. Dr. Alzheimer later described Auguste as having an aggressive form of dementia, manifesting in memory, language and behavioral deficits³. Dr. Alzheimer noted many abnormal symptoms, including difficulty with speech, agitation, and confusion⁴. He followed her care for five years, until her death in 1906. Following her death, Dr. Alzheimer performed an autopsy, during which he found dramatic shrinkage of the cerebral cortex, fatty deposits in blood vessels, and atrophied brain cells². He discovered neurofibrillary tangles and senile plaques,

which have become indicative of AD⁴. The condition was first discussed in medical literature in 1907 and named after Alzheimer in 1910.

Alzheimer's Disease vs. Dementia and Normal Aging

Alzheimer's disease is often confused with normal aging and dementia. Severe memory loss, characteristic of AD, is not a symptom of normal aging. Healthy aging may involve the gradual loss of hair, weight, height and muscle mass. Skin may become more fragile and bone density can be lost. A decrease in hearing and vision may occur, as well as a decrease in metabolic rate. It is common to have a slight decline in memory, such as slower recall of information, however cognitive decline that impacts daily life is not a normal part of the aging process⁵.

Dementia is defined as the significant loss of cognitive abilities severe enough to interfere with social functioning⁶. It can result from various diseases that cause damage to brain cells. There are many different types of dementia, each with its own cause and symptoms. For example, vascular dementia is caused by decreased blood flow to a part of the brain, as caused by a stroke. Dementia may also be present in patients with Parkinson's disease and hydrocephalus. AD is the most common form of dementia, caused by the build-up of beta amyloid plaques in the brain¹.

Disease Presentation

AD progresses gradually and can last for decades. There are three main stages of the disease, each with its own challenges and symptoms. By identifying the current stage of the disease, physicians can predict what symptoms can be expected in the future and possible

courses of treatment. Each case of AD presents with a unique set of symptoms, varying in severity.

Early-Stage Alzheimer's disease

This mild stage, which usually lasts 2 to 4 years, is often when the disease is first diagnosed. In this stage, family and friends may begin to realize that there has been a decline in the patient's cognitive ability. Common symptoms at this stage include^{2,7}:

- Difficulty retaining new information
- Difficulty with problem solving or decision making. Patients may start to have trouble managing finances or other instrumental activities of daily living.
- Personality changes. The person may begin to withdraw socially or show lack of motivation.
- Difficulty expressing thoughts
- Misplacing belongings or getting lost. The patient may have difficulty navigating in familiar surroundings.

Moderate Alzheimer's Disease

Lasting 2 to 10 years, this is longest stage of the disease. Patients often experience increased difficulty with memory and may need help with activities of daily living. Symptoms frequently reported during this stage include^{2,7}:

- Increasingly poor judgment and confusion. The patient may begin to confuse family members, lose orientation to time and place, and may begin wandering, making it unsafe for them to be left alone.

- Difficulty completing complex tasks, including many of the instrumental activities of daily living, such as managing finances, grocery shopping, planning, and organization.
- Greater memory loss. Patients may begin to forget details of their personal history.
- Significant personality changes. The person may become withdrawn from social interactions and develop unusually high suspicions of caregivers.

Severe Alzheimer's Disease

In this final stage of the disease, cognitive capacity continues to decline and physical ability is severely impacted. This stage can last between 1 and 3 years. Due to the family's decreasing ability to care for the patient, this stage often results in nursing home or other long term care facility placement. Common symptoms appearing in this stage include^{2,7}:

- Loss of ability to communicate. The patient may still speak short phrases, but are unable to carry on a coherent conversation.
- Reliance on others for personal care, such as eating, bathing, dressing, and toileting. Many patients become incontinent.
- Inability to function physically. The person may be unable to walk or sit independently. Muscles may become rigid and swallowing can eventually be impaired.

Changes in the Brain

AD causes two distinct deformities in the brain, neurofibrillary tangles and senile plaques. The neurofibrillary tangles are found in the cytoplasm of neurons in the entorhinal cortex. There are two different kinds of plaques, neuritic and diffuse. Neuritic plaques are spherical structures that contain neurites, which are surrounded by an abnormal protein known as

amyloid³. Diffuse plaques lack neurites and have an amorphous appearance. Both types of plaques are found in the neocortex of the brain.

As the number of plaques and tangles increases, healthy neurons begin to function less effectively. The neurons gradually lose their ability to communicate and consequently die, resulting in an overall shrinkage of brain tissue. Neuron death, particularly in the hippocampus, restricts the patient's ability to form new memories.

Death from Alzheimer's Disease

Deaths from Alzheimer's disease as the underlying cause have increased dramatically since 1991. The changes in the brain caused by AD are not usually the primary cause of death. AD often causes complications, such as immobility and trouble swallowing. These can lead to malnutrition and increased risk of pneumonia, resulting in death in these patients¹.

Risk Factors

Age

The single greatest risk factor for developing Alzheimer's disease is age. Most cases of AD are seen in older adults, ages 65 years or above. Between the ages of 65 and 74, approximately 5 percent of people have AD. For those over 85, the risk increases to 50 percent².

Genetics

In sporadic AD, there does not appear to be a genetic pattern of inheritance. A connection has been found between a gene called Apolipoprotein E (ApoE) and the development of AD. This gene is responsible for the protein that carries cholesterol in the blood. One form of the

gene, ApoE4, has been shown to increase the chances of developing the disease. However, the ApoE2 form protects from the disease^{7,8}.

In the cases occurring before age 65, a mutation of chromosomes may be to blame. This rare form of the disease is called Familial Alzheimer's disease and it affects less than 10 percent of AD patients. It is caused by mutations on chromosomes 1, 14, and 21. If one chromosome mutation is inherited, the person will most likely develop AD. Offspring have a 50 percent risk^{9,10}.

Education

There may be a connection between educational level and the risk of developing AD. People with fewer years of education seem to be at a higher risk. The exact cause for this relationship is unknown, but it is theorized that a higher education level leads to the formation of more synaptic connections in the brain. This creates a "synaptic reserve" in the brain, enabling patients to compensate for the loss of neurons as the disease progresses^{1,7}.

Coexisting Health Problems

There is a strong link between cardiovascular health and brain health. Having heart disease, high blood pressure or high cholesterol can increase the risk of developing AD. This is caused by damage to blood vessels in the brain, resulting in less blood flow and possible brain tissue death. Type 2 diabetes may also increase the risk for AD. Inefficiency of insulin to convert blood sugar to energy may cause higher levels of sugar in the brain, causing harm.

Diagnosis

Diagnostic Criteria

The only method of definitively diagnosing AD is a brain autopsy. However, mental and behavioral tests and physical examinations allow physicians to make an accurate diagnosis of AD in 90 percent of cases⁸. The criterion for diagnosing mental disorders can be found in the Diagnostic and Statistical Manual of Mental Disorders (DSM-III), published by the American Psychiatric Association. In this manual, AD falls into the category of primary degenerative dementia. The diagnostic criterion includes dementia, insidious onset with progressive deterioration, and exclusion of all other types of dementia by history and physical examination⁹. A diagnosis of dementia includes a loss of intellectual abilities severe enough to interfere with social or occupational functioning, memory impairment, and a variety of other symptoms⁹.

The first step in finding a diagnosis is obtaining the patient history. During this time, the physician will determine what symptoms are present, when they began, and how they have progressed over time. The family history of illness is also pertinent. The physician will perform a physical examination, including blood tests and urinalysis. This is done to rule out other potential causes of dementia, such as hormone imbalance, vitamin deficiency, and urinary tract infections. Brain scans may also be performed to exclude tumors, cerebrovascular accidents, traumatic brain injury, and infections. These scans are also helpful in identifying the characteristic tangles and plaques seen in AD. Structural imaging scans, including magnetic resonance imaging (MRI) and computed tomography (CT), provide information about the shape and volume of the brain. Functional imaging allows the physician to determine how effectively the brain cells are working. A functional MRI or positron emission tomography (PET) scan can be used¹⁰.

Neuropsychological examinations may be used to identify cognitive symptoms. The most commonly administered test is the Mini-Mental State Exam (MMSE). The physician begins by asking a series of questions designed to test the patient's ability to recall and name a list of objects, perform simple arithmetic, and follow instructions. The patient is then assigned a score out of 30 possible points, with a score of less than 12 indicating severe dementia. AD patient's scores typically decrease 2 to 4 points every year².

The physician may also use the Alzheimer's disease Assessment Scale (ADAS) to measure the severity of the disease. The ADAS evaluates the patient's orientation, memory, reasoning and language on a scale of 0 to 70. A higher score represents a higher level of cognitive impairment. The cognitive portion of the ADAS is sensitive to a wide array of symptoms and assesses many cognitive skills, including spoken language ability, recall of instructions, ability to find correct words, following commands, and orientation to surroundings and time¹⁰.

In addition to mental tests, the doctor may perform a neurological exam to assess the function of the patient's brain and nervous system. This exam will test reflexes, coordination and balance, sensation, muscle strength, speech, and eye function.

Detection Techniques

Neuroimaging is a promising area of research for detecting AD. There are multiple brain imaging procedures that can be used to identify abnormalities in the brain, including PET, MRI, and CT scans. Each scan involves a unique technique and detects specific structures and abnormalities in the brain. Brain imaging is not currently a standard part of AD testing, however

current clinical studies have shown promising results that may change the procedure used by physicians to diagnose the disease.

PET

Positron emission tomography (PET) uses radiation signals to create a three-dimensional color image of the human body¹¹. The patient is injected with a radiotracer, composed of a radioactive medicine bound to a naturally occurring chemical. For the study of AD, the chemical is usually glucose. The radiotracer travels to the organs that use that specific molecule for energy. As the compound is metabolized, positrons are emitted. The energy from these positrons is detected by the PET scan, which converts the input to an image. This image reflects the function of the patient's body by showing how effectively the radiotracer is broken down. The amount of positron energy emitted creates a variety of colors and intensities, which reflects the extent of brain activity. A PET scan has the capacity to detect changes in metabolism, blood flow, and cellular communication processes in the brain¹¹.

A study published in the 1996 Journal of Clinical Psychiatry described the method of using a PET scan to detect the changes in glucose metabolism in the brain of an AD patient. In the parietal, temporal, and posterior cortices, an abnormally low metabolic rate of glucose was found. The rate was further decreased in patients who had an advanced stage of the disease and affected more locations in the brain¹². Small and his colleagues discovered that a PET scan could be used to detect the changes in glucose metabolism well before the clinical presentation of symptoms. In addition to diagnosis, a PET image could also be implemented in determining the effectiveness of AD treatments¹³.

PET Pros and Cons

A PET scan can be an effective choice for diagnosing AD because it can detect multiple metabolic processes and can be used with several different labels. However, this procedure is invasive in that it requires the use of radioactive isotopes. The resolution produced on the image is also limited by the type of radiotracer used¹⁴.

PET Accuracy

PET scans that test the utilization of glucose in the brain have produced accurate diagnoses in ninety-percent of AD cases studied, according to a study at the University of Utah¹⁴. This technique uses a radiotracer called fluorodeoxyglucose (FDG), which mimics glucose in the body. The scan then detects how well the tracer is metabolized in the brain. This technique is especially effective in distinguishing between frontotemporal dementia (FTD) and AD. In cases of FTD, decreased glucose metabolism will be seen in the front of the brain. Abnormalities in AD are seen in the back of the brain¹⁴. The researchers concluded that the addition of this test to the clinical diagnostic criteria would increase the accuracy of diagnosis.

CT

A computed tomography (CT) scan takes a series of cross-sectional images of the body¹⁵. With the help of a computer, the individual scans are integrated into one detailed image. The CT scan provides the physician with information about the density of tissues in the body. For improved clarity, a contrast dye may be injected to provide a distinction between similar tissues³.

CT Pros and Cons

A CT scan is one of the most reasonably priced neuroimaging techniques available. It is a quick and painless procedure and can produce detailed images of bone and soft tissue. However, several risks do exist with this system. The patient may have an allergic reaction to the dye used and is exposed to radiation. The test results may also be misinterpreted and cannot be utilized for every disease.

CT Accuracy

CT scans can be accurate in diagnosing AD and ruling out other possible causes of the symptoms. However, this type of scan is more effective during the later stages of the disease. This technique is most often used to identify the neurofibrillary tangles and beta-amyloid plaques seen during advanced stages of AD. In early diagnosis, research has shown that both the MRI and PET scans are more effective.

MRI

Magnetic resonance imaging (MRI) techniques, first used in 1977, create two or three-dimensional images of the body that can be used to diagnose injury and illness. The essential component of the MRI system is the superconducting magnet, which produces a large and stable magnetic field¹⁶. There are smaller gradient magnets that create weaker magnetic fields. These magnets allow for different parts of the body to be scanned. The human body is composed of billions of atoms. However, it is the hydrogen atoms that are altered by the magnetic field. Hydrogen atoms are each randomly spinning around an axis, but inside the magnetic field of the MRI, the molecules are lined up with the direction of the field. Half of the atoms point towards the patient's head, and half point toward the feet, cancelling each other out. A few atoms out of

every million are not cancelled out. The machine then emits a radio frequency pulse specific to hydrogen, which causes these protons to spin in a different direction. When the spinning ceases, the protons release energy, which is interpreted by the system. Using a contrast dye, each type of tissue responds differently and appears as a unique shade of gray when the image is created¹¹.

Knowing how the system works, researchers are able to determine if an MRI can effectively detect the structural changes and cellular death seen in the brain of an AD patient. Atrophy of the hippocampus is often seen in AD, even before the appearance of clinical symptoms¹⁰. The Nun Study, conducted in 2002, collected postmortem MRI scans of 56 participants with varying degrees of cognitive impairment. The MRI was used to detect the hippocampal volume and determine its significance as an indicator of AD neuropathology¹⁷. The results indicated that the scans could be used to identify non-demented elderly with AD neuropathology who have not yet presented with memory impairment. By identifying the risk for these patients to develop AD well before the appearance of symptoms, physicians may be able to administer treatment to slow the progression of the disease.

A more recent study conducted in 2009 by the Departments of Radiology and Neurology at the University of Pennsylvania investigated the use of sodium magnetic resonance imaging in the detection of AD. This imaging technique uses the same principle as discussed above. However, instead of measuring the hydrogen atoms, this technique uses naturally abundant sodium, ²³Na. This ion was chosen because of the ability of sodium in the brain to detect tumors and track cell death¹⁸. The participants included five healthy elderly adults and five who had a probable diagnosis of AD. When neuronal death occurs, the intracellular space is decreased. Therefore, there is an increased concentration of sodium in the extracellular space, causing stronger signal intensity from the MRI for patients who have AD. Though this technique is not

yet perfected, studies are being conducted to determine if the increased signal intensity is caused by a change in ion concentration or a change in volume¹³.

MRI Pros and Cons

When considering the effectiveness of this technique, there are both pros and cons. Potential benefits of choosing this procedure are that it is painless and can detect very minute abnormalities without the radiation exposure of an X-ray. The resulting image also has high spatial resolution. However, this process is very expensive and may not be covered by insurance. The space inside the machine is very small, which may make it hard to examine a claustrophobic patient. If a patient has metallic objects inside of their body, they cannot use the MRI system due to the strong magnetic field.

MRI Accuracy

A study conducted by the Florida Alzheimer's Disease Research Center found that MRI scans are effective in detecting the brain atrophy seen in AD. They collected brain scans for 260 participants, some with mild cognitive impairment, others with probable AD, and a control group of elderly adults with no memory decline. The researchers were able to match the scans with the correct group of patients based on the amount of atrophy in the mid-brain. Some scans showed brain loss before any symptoms were present, indicating that this technique would be effective for early diagnosis of the disease¹⁹.

Treatment of Alzheimer's Disease

There is currently no cure for AD, however there are multiple drugs that have been proven to slow disease progression and treat symptoms. When initiating treatment for AD patients, physicians divide the symptoms into “cognitive” and “behavioral and psychiatric” categories². This enables treatment that is specific to the symptoms being experienced. Cognitive symptoms affect memory, language, judgment, and thought processes. Behavioral symptoms alter a patient's actions and emotions.

Treatment for Cognitive Symptoms

Treatment of cognitive symptoms involves altering the affect of chemical messengers in the brain. The Food and Drug Administration (FDA) has approved two types of medication for this purpose². The first type is called a cholinesterase inhibitor, which hinders the enzyme responsible for the breakdown of acetylcholine in the brain. Acetylcholine is an important neurotransmitter involved in learning and memory. Normal aging causes a slight decrease in acetylcholine concentration, causing periodic forgetfulness. However, in AD, the concentration can be decreased by as much as ninety-percent, resulting in significant memory and behavioral decline²⁰. The function of these drugs is to support communication between nerve cells, therefore increasing the concentration of acetylcholine. There are currently three cholinesterase inhibitors commonly prescribed: donepezil, galantamine, and rivastigmine.

In addition to cholinesterase inhibitors, a medication called memantine has also been approved for the treatment of AD. Memantine regulates the activity of glutamate in the brain. Glutamate is an excitatory neurotransmitter involved in learning and memory²¹. Overstimulation of nerves by glutamate may be the cause of the neuron degeneration seen in AD, called

excitotoxicity²². Glutamate binds to N-methyl-D-aspartate (NMDA) receptors on the surface of brain cells. Memantine functions by blocking the NMDA receptors and therefore protecting the nerves from excessive glutamate stimulation²³. Memantine is indicated in the treatment of moderate to severe AD and can temporarily delay worsening of cognitive symptoms.

Table 1: Overview of Potential Treatments for AD²⁴

Drug Name	Indication	Action	Dose
Donepezil Brand Name: Aricept	Mild to severe AD	Prevents the breakdown of acetylcholine (ACh) by inhibiting the action of acetylcholinesterase Treats cognitive symptoms of AD	5 mg taken once daily Over time, may increase to 10 mg daily
Galantamine Brand Name: Razadyne	Mild to moderate AD	Prevents the breakdown of acetylcholine and stimulates receptors to release excess ACh Treats cognitive symptoms of AD	4 mg taken twice daily Over time, may increase to a maximum of 24 mg daily
Rivastigmine Brand Name: Exelon	Mild to moderate AD Also used to treat dementia from Parkinson's Disease	Prevents the breakdown of acetylcholine by inhibiting the enzymes that degrade ACh Treats cognitive symptoms of AD	1.5 mg taken twice daily Over time, may increase to a maximum of 12 mg daily
Memantine Brand Name: Namenda	Moderate to severe AD	Blocks glutamatergic (NMDA) receptors and regulates the action of glutamate Treats cognitive symptoms of AD	5 mg taken once daily Over time, may increase to a maximum of 10 mg daily

Table 1 continued: Overview of Potential Treatments for AD²⁴

Drug Name	Adverse Effects	Contraindications
Donepezil Brand Name: Aricept	CNS: headache, seizures, insomnia, fatigue, aggression CV: chest pain, hypertension, atrial fibrillation GI: nausea, vomiting, GI bleeding Metabolic: Weight loss, dehydration	Do not use in patients that are hypersensitive to the drug Use caution in patients with cardiovascular disease, asthma, COPD, ulcer disease, or patients taking NSAID pain relievers
Galantamine Brand Name: Razadyne	CNS: depression, dizziness, fatigue, insomnia CV: bradycardia, AV block GI: diarrhea, nausea, anorexia, abdominal pain Hematologic: anemia	Do not use in patients that are hypersensitive to the drug Use caution in patients that have cardiac conduction disorders, before procedures requiring anesthesia, and in patients with ulcer disease, seizures, or asthma
Rivastigmine Brand Name: Exelon	CNS: headache, dizziness, confusion, nervousness, paranoia, malaise CV: hypertension, chest pain, edema Musculoskeletal: back pain, bone fractures Respiratory: bronchitis, cough	Do not use in patients that are hypersensitive to the drug Use caution in patients with GI bleeding, cardiovascular disease, COPD, or seizure disorders
Memantine Brand Name: Namenda	CNS: stroke, aggressiveness, agitation, fatigue, confusion, pain, syncope CV: heart failure, edema GI: anorexia, constipation, nausea, vomiting Skin: Rash	Do not use in patients that are allergic to the drug or its components Not recommended for mild AD or in patients with renal impairment Use caution in patients with seizures or increased urine pH

Donepezil hydrochloride (Brand name Aricept)

This medication has been approved to treat all stages of AD by preventing the breakdown of acetylcholine in the brain. Donepezil is a highly selective and reversible antagonist for acetylcholinesterase (AChE). The pharmacology profile and long half life allow for a once daily dosage. A study published in the 1998 Archives of Internal Medicine examined the effects of this

treatment on 468 participants. The patients had mild to moderate AD according to results from the MMSE and Clinical Dementia Ratings²⁵. The study excluded patients with any coexisting medical conditions that might interfere with the trial. The participants were divided into three groups. One group received two placebo tablets. Another group received one placebo tablet and one 5-mg donepezil tablet. The final group received two 5-mg donepezil tablets. Among the groups receiving the drug, 32% of the 5-mg treatment group and 38% of the 10-mg treatment group showed clinical improvement on various psychiatric and mental scales. Donepezil is the only cholinesterase inhibitor approved to treat severe AD. Overall, research has shown that this drug is effective at slowing cognitive decline.

Galantamine hydrobromide (Brand name Razadyne)

Galantamine is indicated in the treatment of mild to moderate AD by blocking the hydrolysis and increasing the concentration of acetylcholine. Unlike donepezil, galantamine must be administered twice daily due to a short half life of only seven hours²⁴. A research study conducted by Loy and Schneider investigated the effect of galantamine on cognitive symptoms at three and six month intervals²⁶. Patients taking doses of 18-32 mg/day showed significant improvements at both time intervals. The effects were greater after six months of treatment and were effective at improving the cognitive examination scores of the participants²⁶. A meta-analysis of AD treatment studies by Hansen and a group of researchers found that galantamine is able to slow the decline of cognitive function with adverse effects occurring in a small percentage of participants²⁷.

Rivastigmine tartrate (Brand Name Exelon)

This medication is prescribed less frequently than other cholinesterase inhibitors for the treatment of mild to moderate AD. A study conducted by the Department of Psychiatry at the Sunnybrook Health Sciences Center in Toronto examined the effectiveness of rivastigmine at various dosages and time periods²⁸. A lower dose of 1-4 mg/day and a higher dose of 6-12 mg/day were tested at 12, 18, and 26 week intervals. The group taking the highest dosage showed the greatest improvement in cognitive examination scores and activities of daily living over all time intervals. The lower dosage showed improvement only after the 26 week duration and did not alter the activities of daily living ability. Side effects were experienced in a small percentage of participants taking the higher dosage when compared to the placebo. Overall, this drug has been proven to be effective in treating the cognitive symptoms of AD when taking 6-12 mg daily over a long period of time²⁸.

Memantine (Brand Name Namenda)

Memantine is a NMDA receptor antagonist approved for the treatment of moderate to severe AD²⁴. According to a study published in the 2003 New England Journal of Medicine, memantine-induced regulation of NMDA receptors resulted in a decrease in deterioration and alleviation of AD symptoms²². Of the 345 participants initially screened, 181 completed the 28-week double-blind trial. The participants were fifty years of age or above with a diagnosis of moderate to severe AD. Each also had CT and MRI scans within the previous 12 months. Twenty-nine percent of the memantine group and ten percent of the placebo group showed a positive response to the medication. There were adverse effects in nearly all of the participants, although most were unrelated to the medication. The most common side effect was agitation. Although this trial showed results in fewer participants, this was to be expected compared to

studies of cholinesterase inhibitors. Those trials were conducted on patients with mild to moderate AD, making them more likely to show improvement following treatment²². Overall, the data obtained indicates that memantine can effectively reduce deterioration in patients with advanced AD.

Treatment for Behavioral and Psychiatric Symptoms

In addition to cognitive and functional decline, AD can cause severe behavioral and psychiatric symptoms. These symptoms include anxiety, sleeplessness, agitation, hallucinations, and delusions²⁹. Possible treatment methods involve non-drug interventions and medications to treat the symptoms being presented. Altering the environment to eliminate obstacles and increase security is an effective non-drug approach². Another possibility is investigating any potential interactions between the patient's medications that could cause adverse effects to behavior or psychiatric health. If these interventions do not improve the symptoms, medication may be required. There are multiple medications that could be chosen depending on the symptoms. For example, if the patient is experiencing depression, an antidepressant such as Prozac or Zoloft can be prescribed. Antipsychotics and anxiolytics may be taken to reduce hallucinations and anxiety, respectively².

The Economic Affect of Alzheimer's Disease

The cost of AD amounts to \$172 billion annually. AD patients utilize a large amount of healthcare, hospice, and long term care (LTC) facilities. In 2004, Medicare payments for AD patients aged sixty-five and older were three times greater than patients without AD, costing \$15,145 and \$5,272, respectively¹. For Medicaid, which pays for individuals with low income and assets, the cost is nine times higher for patients with AD.

Use of Healthcare Services

Patients with AD use more healthcare services and typically require more expensive care. The table below summarizes the differences between usage and costs for people with AD or dementia and other elderly individuals. This table was created using data from the 2009 Characteristics, Costs and Health Service Use for Medicare Beneficiaries with a Dementia Diagnosis Report³⁰.

Table 2: Average Use of Healthcare Services by People With and Without AD or Dementia³⁰

Healthcare Setting	AD vs. Other Elderly Usage	Average Cost for AD Patient	Average Cost for Other Elderly
Hospital	AD 3 times more visits	\$7,663	\$2,748
Skilled Nursing Facility	AD 8 times more likely to require service	\$3,030	\$333
Home Health Care	AD 2 times more likely to require service	\$1,256	\$282

A large majority of hospital admissions for people with AD are preventable if an accurate diagnosis is made early. One study of people over age 70 published by the Alzheimer's Association showed that those with cognitive impairment who were given a diagnosis of AD by their physician had significantly fewer hospitalizations than those who had not been accurately diagnosed¹. This indicates that by proper training of physicians and implementation of new diagnostic techniques, AD can be effectively diagnosed and managed without incurring the high cost of hospital care.

Most AD patients have one or more co-morbid conditions that cause an increase in the cost of healthcare. Sixty percent of AD patients have hypertension. Twenty-six percent have

coronary heart disease and twenty-five percent have had a stroke¹. These medical conditions increase the number and length of hospital admissions, as well as the cost of treatment. A large percent of these diseases are preventable by proper patient education. Diet and exercise can drastically reduce the incidence of hypertension, cardiovascular disease, and diabetes.

Decreasing the prevalence of co-morbidities may also reduce the need for LTC placement, increasing autonomy for the patient. A few simple lifestyle changes can improve the quality of life for patients with AD and their families.

Living Arrangements

About seventy percent of people with AD live at home and are cared for by family and friends. Many of these individuals are in the advanced stages of the disease and may require additional paid non-medical home care. This includes assistance with bathing, dressing, cleaning, cooking, and shopping. About thirty-seven percent of elderly adults receiving home care have AD or some form of dementia¹. Other adults with AD may also choose to utilize adult day care services.

Individuals with advanced AD who require care beyond the capabilities of family members are often placed in assisted living (ALF) or skilled nursing (SN) facilities. It is estimated that between forty-five and sixty-seven percent of ALF residents have AD or dementia. In 2009, forty-nine percent of all SN facility residents had a diagnosis of AD, while another twenty-seven percent had mild cognitive impairment¹. Some nursing homes have special Alzheimer's Care Units, accounting for five percent of the total number of nursing home beds. Below is a table summarizing the costs of care for each type of setting for individuals with AD.

The table was created using data obtained from the 2010 Alzheimer's Disease Facts and Figures Report by the Alzheimer's Association¹.

Table 3: Average Cost for Individuals with AD Depending on Type of Care Setting¹

Type of Care Setting	Average Cost for AD Patient	Medicare Coverage
Home Care	\$19 per hour, \$152 for eight-hour day	Yes: 100 visits
Adult Day Care	\$67 per day, some charge additional fee for AD patient care	No
Assisted Living Facility	\$4,435 per month for AD patient care, \$53,220 per year	No
Skilled Nursing Facility	\$219 per day for private room, \$79,935 per year \$198 per day for semi-private room, \$72,270 per year	Yes: 100 days following hospitalization of three days minimum
Alzheimer's Care Unit	\$233 per day for private room, \$85,045 per year \$208 per day for semi-private room, \$75,920 per year	No: this is usually a long term care placement, which is not covered

Even with Medicare and Social Security, these costs are astronomically high and most individuals with AD cannot afford them. In 2005, it was estimated that sixty-five percent of older adults in the United States had assets that could not pay for a year in a nursing home¹.

Additionally, fifty-seven percent of the elderly in the community could not afford even one month of long term care.

Affording Long Term Care

Programs such as Medicare, Medicaid, and long term care insurance can help an individual pay for the cost of living and medication, provided the patient meets certain criteria. In 2002, it was estimated that six million people had long term care insurance, which paid \$1.4 billion dollars that year¹. The cost of LTC insurance varies depending on the individual's age at the time of purchase and the coverage selected. For example, a person may choose to purchase comprehensive care with a lifetime maximum benefit of \$200,000. The monthly premium is determined by the applicant's age at purchase and remains constant over time. This person will receive a certain amount of money every month during the illness or disability until reaching the maximum allotment. However, there are a few limitations to this insurance. If you are already living in a LTC facility, have dementia or AD, or need assistance with activities of daily living, you will most likely be denied coverage³¹. This is why early detection of the risk of developing AD is crucial. The individual must plan for the future and purchase the insurance before symptoms appear. Once the plan is approved, coverage cannot be cancelled due to health issues. Being educated about one's personal risk for developing AD and deciding to purchase early can make a huge difference in the ability to pay for long term care.

Medicare is a governmental health insurance program established in 1965 for adults aged sixty-five years and older and certain individuals with disabilities. Medicare has two main portions. Part A covers hospital expenses and some skilled nursing and home care. Most individuals do not have to pay for Part A because they paid Medicare taxes during employment. Part A will cover up to 90 days of a hospital stay and 190 days for psychiatric care during the beneficiary's lifetime². Skilled nursing care may be covered for up to 100 days, provided the beneficiary was admitted to the hospital for at least three days prior. Medicare Part B is medical

insurance that covers visits to the doctor, outpatient hospital procedures, and physical or occupational therapy³². This portion requires a monthly premium. An individual who has both Parts A and B may receive 100 home health visits, including nursing care and therapy. Hospice care is covered by Medicare in patients who are terminally ill and expected to pass away within six months. The individual may also choose to add the Medicare Prescription Drug Plan to assist in purchasing medication. Medicare will pay for the diagnosis and treatment of AD, but will not cover adult day care, personal aides, incontinence supplies, and experimental treatments².

Medicaid is a form of health insurance that covers expenses when individuals cannot afford to pay their medical bills. Medicaid provides coverage to a wide variety of people, including pregnant women and newborns, people with disabilities, and individuals and families with limited income³³. Need is based on income within a certain percentage of the federal poverty guidelines. Medicaid will pay the premium for Medicare Part B for individuals with low income and can pay in the event that a person has already utilized certain Medicare benefits. The majority of Medicaid spending, nearly seventy-five percent annually, goes towards LTC services³⁴. Due to lack of awareness, this program is underutilized, with only one-third of poor elderly claiming benefits.

Improving Quality of Life for the Patient and Family

There are multiple ways in which the research presented can be beneficial for an individual with AD and their family and friends. The patient may profit economically, emotionally, and physically from an early diagnosis of AD. Once a diagnosis is made, it is imperative that the correct course of treatment be implemented to delay further brain deterioration and slow the onset of symptoms.

The most obvious way that an individual with AD can benefit is monetarily. AD diagnosis and treatment can be very costly. Early diagnosis would allow the patient to make arrangements for the future. If the risk of developing AD was discovered before the appearance of symptoms, LTC insurance could be purchased, drastically decreasing the amount of money needed for living and medical costs. Another economic benefit is the ability to start saving money to cover expenses not paid by Medicare and other insurance plans. By educating adults about the options available after retirement, the financial burden of AD can be diminished. Individuals need to understand the importance of planning for the future before the appearance of a serious illness.

Early diagnosis also benefits the patient in a personal way. Everyone has goals for their lives, but due to the debilitating symptoms of AD and dementia, patients may not be able to achieve them. An early diagnosis followed by treatment could allow the individual to make plans for the future and accomplish their goals before the disease progresses. In many cases, AD patients do not have the opportunity to make decisions before severe cognitive symptoms appear. This responsibility often falls to the children. New diagnostic techniques, such as MRI and PET scans, can allow older adults to decide their course of treatment and living arrangements before the disease progresses. This includes writing advanced directives and wills so that the patient's wishes will be honored despite their cognitive state. The patient can also make living arrangements, such as choosing which LTC facility or home health agency to use in the future.

Maintaining autonomy is one of the main goals of AD research. Early diagnosis and treatment can delay symptoms for up to 12 months, helping to maintain thinking skills and memory. This additional symptom-free time enables the patient to remain in their own home near family and friends. Patients can maintain autonomy in activities of daily living, enhancing

their quality of life. Another important factor is the ability to spend quality time with family and friends. AD can progress quickly, causing the patient to forget the people around them. It is beneficial for the patient as well as the family to have this precious time together while they are still capable.

AD takes an emotional toll on both the patient and family members. It is incredibly difficult to watch a loved one deteriorate and forget how to perform the activities they once loved. It is confusing and aggravating for the patient to be unable to care for themselves and not recall familiar information. Additional time due to an early diagnosis is crucial for the emotional health of everyone involved. Families can be given adequate time to accept what is happening and discuss their feelings. This can relieve some of the anxiety related to the unknown future and make the patient's final years of cognitive stability more enjoyable.

The final benefit derived from an early diagnosis is education of the patient and family. The patient first needs to be educated about the disease, including progression of symptoms, treatments available, and what to expect in the future. Family members can receive counseling to decide the best course of action for dealing with the changes they will experience. Knowing what symptoms to expect can enable the patient to make changes to their home environment. AD patients tend to wander when they are confused. Increasing safety and eliminating obstacles in the home allows patients to remain there for a longer period of time. The FDA has approved four treatments for AD and is currently conducting research studies on many more. Early diagnosis can allow patients to enter these clinical trials and have a greater chance of benefiting from the treatment. A longer symptom-free period allows the patient and family to make an educated decision regarding treatment.

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