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**Fun Fact:** According to the Alzheimer's Association, their signature color is purple. This color combines the calm stability of blue and the passionate energy of red. It shows that the association and their supporters are strong and unrelenting in the fight against Alzheimer's disease.<sup>1</sup>



- What is Alzheimer's disease?
- How common is Alzheimer's disease?
- Non-pharmacologic treatment options for Alzheimer's disease.
- Drugs approved for the treatment of Alzheimer's disease.
- BREAKING NEWS!

#### What is Alzheimer's Disease?

Alzheimer's disease is a type of dementia. In fact, it is the most common type of dementia. It is a progressive disease involving the areas in the brain that control thought, memory, and language. It starts as mild memory loss and progresses to loss of the ability to respond to the environment and hold a conversation, so it can seriously impair a person's ability to carry out daily activities. The cause of Alzheimer's disease is not fully understood. Multiple factors play a role in its development, and each of these factors affects each person differently. Some risk factors for Alzheimer's include age, family history, changes in the brain, and environmental factors.<sup>2</sup>

#### 10 Warning Signs of Alzheimer's:<sup>2</sup>

- 1. Memory loss that disrupts daily life.
- 2. Challenges in planning or solving problems.
- 3. Difficulty completing familiar tasks at home, at work, or at leisure.
- 4. Confusion with time or place.
- 5. Trouble understanding visual images and spatial relations.
- 6. New problems with words in speaking or writing.
- 7. Misplacing things and losing the ability to retrace steps.
- 8. Decreased or poor judgment.
- 9. Withdrawal from work or social activities.
- 10. Changes in mood and personality.

#### **How Common is Alzheimer's Disease?**

The estimates vary, but around 6 million Americans aged 65 years or older are estimated to have Alzheimer's disease, or 1 in 9 people. The size of the U.S. population aged 65 years or older is continuously growing, so the prevalence rate of Alzheimer's disease is increasing. The Alzheimer's Association estimated that the number of people aged 65 years or older with Alzheimer's disease may be 12.7 million by 2050 if there is no development of Alzheimer's disease prevention or cure. Furthermore, small numbers of young adults in their 30s to 40s have developed Alzheimer's disease, which is known as early-onset (younger-onset) Alzheimer's disease. Thus, it is crucial to proceed with an efficient medical care process (non-pharmacologic and pharmacologic) in advance to decrease the rate of Alzheimer's disease. 3,4

#### Non-Pharmacologic Treatment Options for Alzheimer's Disease

There are several options for treating Alzheimer's disease other than pharmacologic intervention. As the disease progresses, it becomes more difficult for patients to spend their daily lives alone. Options for non-pharmacologic intervention depend on these patient factors: symptoms, severity, and the duration of disease progression.<sup>5</sup>

<u>Cognitive Therapy:</u> Cognitive therapy aims to help improve mental abilities like perception, thinking, and memorization. It can temporarily improve mental performance and language ability in mild to moderate Alzheimer's disease.

<u>Physical / Social Stimulation:</u> Physical and social stimulation aims to improve a patient's ability to complete various activities such as brushing their teeth, wearing clothes, and writing letters. Additionally, they can improve their strength and balance to perform daily activities.

Emotion-Oriented Treatment: Emotion-oriented treatment aims to enhance patients' quality of life by focusing on their feelings, values, and experiences. This approach includes two main types of therapy. The first type is validation therapy, where caregivers use specialized communication skills to build closer connections with patients. In this therapy, caregivers cannot judge patients' disease states, such as their behavioral or mood changes. The primary goal is to create a comfortable and safe environment for patients to communicate openly with their caregivers. The second type of emotion-oriented treatment is reminiscence therapy, which encourages patients to recall and talk about their past experiences such as stories from school, work, and home. This therapy is particularly beneficial for patients with Alzheimer's disease. By engaging patients in discussions about their personal histories, reminiscence therapy aims to mitigate psychiatric effects associated with Alzheimer's disease, such as depression. Some studies show reminiscence therapy can improve patients' moods and mental health. However, these claims are not strong, having minor evidence power. Despite the limited robustness of the existing studies, reminiscence therapy is one of the most valuable non-pharmacologic interventions among patients with Alzheimer's disease.

<u>Diet:</u> Some professionals insist that eating a healthy diet helps to prevent or delay the progress of Alzheimer's disease. The Mediterranean diet is the best example of a healthy diet that improves memory and cognitive function.

In summary, not all non-drug therapies guarantee an improvement in a patient's overall quality of life. While treatments like cognitive therapy may offer benefits, they can also potentially cause side effects such as mood changes, frustration, and confusion. Therefore, it is crucial to have discussions with patients about individual preferences, needs, and potential risks of side effects to determine the most suitable options for non-pharmacological therapy. Potentially, non-pharmacologic interventions may help patients' well-being and maximize the effectiveness of their pharmacologic treatment plan.<sup>5</sup>

#### **Drugs Approved for the Treatment of Alzheimer's Disease**

#### Mild Cognitive Impairment 6,7,8

Drug	MOA	Adverse Reactions	Pearls
Anti-amyloid mAb Aducanumab (Aduhelm)	Monoclonal antibody that works by binding to and reducing beta-amyloid plaques.	- Amyloid-related imaging abnormalities (ARIA)*	Must confirm presence of beta-amyloid plaques prior to treatment.
Lecanemab (Leqembi)	p.mq.mes.	- Diarrhea - Infusion-related reactions	Recommended to undergo genetic testing for Apolipoprotein E \$\epsilon 4\$, carriers of this gene are at higher risk for ARIA.

<sup>\*</sup>There are two different types of ARIA, ARIA-E which is related to cerebral edema and ARIA-H which is related to microhemorrhages within the brain. The presence of ARIA can be detected with MRI.

#### **Mild-Moderate Alzheimer's Disease** 6,7,8

Drug	MOA	Adverse Reactions	Pearls
Cholinesterase Inhibitors Donepezil (Aricept)	Reversibly inhibits acetylcholinesterase centrally; Thus increasing the amount of acetylcholine	- CNS effects (nausea, vomiting, diarrhea) - Decreased appetite	Donepezil and Rivastigmine are available in oral or transdermal dosage
Rivastigmine (Exelon)	in the CNS.	Beereuseu appente	forms; Galantamine is only available as oral.
Galantamine (Razadyne)			

#### **Moderate-Severe Alzheimer's Disease** 6,7,8

Drug	MOA	Adverse Reactions	Pearls
NMDA Receptor Antagonist Memantine (Namenda)	Noncompetitively antagonizes the NMDA receptor; Thus inhibiting overstimulation of glutamate receptors in the brain.	<ul><li>Confusion</li><li>Dizziness</li><li>Drowsiness</li><li>Headache</li></ul>	Available in a tablet or capsule.  **Memantine may be used in combination with Cholinesterase inhibitors.

### Other FDA-approved Medications for Behavioral and/or Psychological Symptoms Associated with Alzheimer's Disease 6,7,8

Indication	Drug	MOA	Adverse Reactions
Insomnia	Suvorexant (Belsomra)	Inhibits the binding of orexin A/B to OX1R and OX2R.	- Headaches - Drowsiness
			- Dizziness
Agitation	Brexpiprazole (Rexulti)	5-HT <sub>1A</sub> / D <sub>2</sub> receptor partial agonist  AND	- ↑ Triglycerides - Weight gain
		5-HT <sub>2A</sub> receptor antagonist	- Akathisia

#### **BREAKING NEWS!**

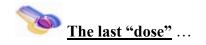
#### New Study Shows a Naturally Occurring Substance Found in Pomegranates Can Improve Treatment of Alzheimer's Disease

A recent study at the University of Copenhagen concludes that a naturally occurring substance called urolithin A, found in pomegranates, strawberries, and walnuts, can improve memory and potentially improve the treatment of Alzheimer's.

When weak mitochondria accumulate in the brain, brain function is affected. Many patients with neurodegenerative diseases, such as Alzheimer's, experience this kind of mitochondrial dysfunction.

The results of this new study show that urolithin A removes weak mitochondria from the brain.

The study used mouse models with AD, so more research is necessary before this knowledge applies to humans, but the prospects are positive. Overall, this is good news for patients with dementia.<sup>9</sup>



## "Though those with Alzheimer's might forget us, we as a society must remember them." - Scott Kirschenbaum [filmmaker]

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