

# Monotherapy vs. Combination Therapy as Long-Term Treatment of Alzheimer's Disease Cognitive Symptoms

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**Background:** Alzheimer's disease is an insidious neurodegenerative disease with cardinal features of gradual cognitive decline and interference in activities of daily living. This disease is pervasive and affects over 10% of the adult population in the United States over the age of 65. Pharmaceutical intervention in the treatment of Alzheimer's disease is usually limited to abating symptoms and slowing decline. Determining the best treatment options to limit cognitive decline, effects on daily life, and any adverse effects that pharmaceutical therapies confer is imperative.

**Purpose:** The goal of this study was to determine if a combination therapy of a cholinesterase inhibitor plus an N-methyl-D-aspartate receptor antagonist is more efficacious at decreasing the symptoms associated with Alzheimer's disease than monotherapy of a cholinesterase inhibitor or N-methyl-D-aspartate antagonist.

**Methods:** Three researchers independently searched Google Scholar, PubMed, and MedLine Complete for systematic reviews and meta-analyses pertinent to the stated purpose. Studies that met inclusion criteria underwent a quality assessment and data extraction, and the researchers ultimately agreed on the 3 most relevant studies of "good" quality for qualitative synthesis.

**Results:** The included systematic reviews and meta-analyses included a total of 81 primary studies ranging from 12 weeks to 3 years. Most studies incorporated donepezil in their design with the most common combination therapy studied being donepezil plus memantine; a cholinesterase inhibitor plus a N-methyl-D-aspartate antagonist, respectively. The evidence from these studies collectively supports the superiority of combination therapy of a cholinesterase

inhibitor plus N-methyl-D-aspartate antagonist for limiting cognitive symptoms and the effects of the disease on the patient's daily life activities. Additionally, combination therapy yields no significantly higher risk of adverse events.

**Conclusion:** Patients presenting with moderate to severe Alzheimer's disease should be placed on a dual therapy regimen of a cholinesterase inhibitor and memantine. Additionally, if either the cholinesterase inhibitor or memantine causes an adverse event, then monotherapy with either a cholinesterase inhibitor or memantine still confers benefit but to a lesser extent than combination therapy.