Dementia Review

Focus on available treatments for Alzheimer’s disease

1. Are there different types of dementia?
2. What are risk factors for developing dementia?
3. How do the cholinesterase inhibitors work and what side effects can be expected?
4. Are generic Razadyne and Aricept just as good?
5. How does Namenda work and what side effects are expected?
6. When should we start treatment for dementia? STOP?
7. Can combinations of medications be used?
8. Is gingko effective?
9. What role do antipsychotics play for behavioral issues associated with dementia?
10. Do any other medications have an impact?
11. What medications can worsen dementia?
12. Summary of Advantages/Disadvantages of treatments options

Agents in this Review:

Cholinesterase Inhibitors (ChEIs)
- Cognex (tacrine)
- Aricept (donepezil)
- Razadyne (galantamine)
- Exelon (rivastigmine)

N-methyl-D-aspartate (NMDA)-Receptor Antagonist
- Namenda (memantine)

Herbals
- Gingko

Highlights: The Quick-Read Information

1. Alzheimer’s disease is the most common form of dementia.
   a. True 
   b. False
2. Which of the following is NOT a risk factor for vascular dementia.
   a. Hypertension 
   b. Diabetes 
   c. History of alcohol abuse 
   d. Atherosclerosis
3. Which cholinesterase inhibitor is associated with the greatest incidence of nausea and vomiting.
   a. Donepezil 
   b. Galantamine 
   c. Rivastigmine
4. Generic medications are inferior to brand medications.
   a. True 
   b. False
5. Ginkgo is an effective treatment option for dementia.
   a. True 
   b. False
6. The FDA has approved the use of antipsychotics for use in patients with dementia.
   a. True 
   b. False
7. Which of the following can worsen dementia.
   a. Atenolol 
   b. Metformin 
   c. Aspirin 
   d. Tolterodine
FDA approved treatment options

<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand Name</th>
<th>Dosage forms</th>
<th>How Supplied</th>
<th>Frequency of administration</th>
<th>IHA Tier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholinesterase Inhibitors (ChEIs)</td>
<td></td>
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<tr>
<td>• All are approved for <strong>mild to moderate</strong> Alzheimer’s disease, Aricept (donepezil) is also approved for <strong>moderate to severe</strong> Alzheimer’s disease</td>
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<tr>
<td>Tacrine</td>
<td>Cognex®</td>
<td>Capsule</td>
<td>10, 20, 30, 40mg</td>
<td>QID</td>
<td>3</td>
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<tr>
<td>Donepezil</td>
<td>Aricept®</td>
<td>Tablet</td>
<td>5, 10mg</td>
<td>QD</td>
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<td>Orally disintegrating tablet</td>
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<tr>
<td>Galantamine</td>
<td>Razadyne®</td>
<td>Tablet</td>
<td>4, 8, 12mg</td>
<td>BID</td>
<td>1(generic) 3(brand)</td>
</tr>
<tr>
<td>Oral solution</td>
<td></td>
<td>4mg/ml</td>
<td>BID</td>
<td></td>
<td>2</td>
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<tr>
<td>Extended release capsule</td>
<td>8, 16, 24mg</td>
<td></td>
<td>QD</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Rivastigmine</td>
<td>Exelon®</td>
<td>Capsule</td>
<td>1.5, 3, 4.5, 6mg</td>
<td>BID</td>
<td>2</td>
</tr>
<tr>
<td>Solution</td>
<td></td>
<td>2mg/ml</td>
<td>BID</td>
<td></td>
<td></td>
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<tr>
<td>Transdermal patch</td>
<td></td>
<td>4.6mg/24hr, 9.5mg/24hr</td>
<td>QD</td>
<td></td>
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<tr>
<td>N-methyl-D-aspartate (NMDA)-Receptor Antagonist</td>
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<tr>
<td>Memantine</td>
<td>Namenda®</td>
<td>Tablet</td>
<td>5, 10mg</td>
<td>QD</td>
<td>2</td>
</tr>
<tr>
<td>Solution</td>
<td></td>
<td>10mg/5ml</td>
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</tr>
</tbody>
</table>

**Are there different types of dementia? → YES**

Mild cognitive impairment is defined as cognitive decline greater than what is expected however does not affect daily activities. Having mild cognitive impairment is associated with a high risk of progressing to full-blown dementia. Treatment with high dose vitamins, NSAIDs and cholinesterase inhibitors have not proven effective. Current recommendations are to manage vascular risk factors such as hypertension, diabetes, hypercholesteremia, and to discontinue any anticholinergic drugs.[1]

Alzheimer’s Disease is the most common form of dementia. The exact cause is unknown however thought to involve many factors. One contribution is the overproduction of beta amyloid, a peptide, and its accumulation into plaques. Additionally, alteration of the tau protein causes destruction of microtubules and formation of neurofibrillary tangles. These mechanisms affect areas of the brain responsible for memory and cognition. Unfortunately there are no treatments to date to deter the previously mentioned causes of Alzheimer’s disease. However, there are two additional causes, excess of excitatory neurotransmitter glutamate and decrease in levels of acetylcholine (ACH), which are targets of therapy. Mainstay of treatment are cholinesterase inhibitors and N-methyl-D-aspartate (NMDA)-receptor antagonist.[1]

The Mini-Mental State Exam (MMSE) is a helpful screening tool; however Alzheimer’s disease can only be confirmed in an autopsy. There are three stages depending on the severity of symptoms. Mild is usually characterized by an MMSE score of 20 to 26 and the patient has difficulty finding correct words, has increased irritability, apathy or depression and/or frequently misplaces objects. At this stage the patient may or not be aware of their condition. Moderate is described when changes in personality, confusion, impaired judgment and difficulty following simple instruction occur. Finally, in the severe stage MMSE is generally below 10 and the patient is very dependent on others for care. Hallucinations, delusions, Parkinson-like symptoms and seizures can occur. Average life expectancy is about 7 years from diagnosis and the range is 2 to 20 years. Death usually occurs due to secondary complications such as infection.[1-2]

Vascular dementia is the second most common cause of dementia. This form is a consequence of inadequate oxygenation of brain tissues, usually due to an infarct. Onset is generally abrupt and treatment is aimed at managing hypertension, diabetes and hypercholesterolemia.[1]

Dementia with Lewy Bodies typically occurs between 50 and 85 years of age. This condition is characterized by large fibrils of a normal brain protein, alpha-synuclein. Symptoms occur as a result of dopamine transporter loss and acetylcholine deficits. Unlike Alzheimer’s disease, memory remains intact and signs/symptoms...
include delirium, variations in attention/alertness, impairment in verbal fluency and visual perception, inability to perform tasks and visual hallucinations. These patients are sensitive to the extrapyramidal adverse effects of antipsychotics therefore if needed it is recommended that low dose atypical antipsychotics be used. Cholinesterase inhibitors have also been used successfully, with Exelon (rivastigmine) having the most evidence.\textsuperscript{[1, 3]}

The onset of Frontotemporal Dementia is early, occurring between the ages of 45 and 60. The cause is unknown however genetics seems to play a role. Symptoms include early decline in social skills, emotional blunting, loss of insight and empathy, compulsive behavior and disinhibition. Memory is generally unaffected until later stages.\textsuperscript{[1]}

**What are risk factors for developing dementia?**\textsuperscript{[1]}

<table>
<thead>
<tr>
<th>Alzheimer’s Disease</th>
<th>Vascular Dementia</th>
<th>Lewy Body Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age&gt; 65 years, female</td>
<td>Hypertension</td>
<td>Age 50-85 years</td>
</tr>
<tr>
<td>Decreased reserve capacity/ brain size</td>
<td>History of stroke</td>
<td></td>
</tr>
<tr>
<td>Low mental ability</td>
<td>Nicotine abuse</td>
<td></td>
</tr>
<tr>
<td>Head injury</td>
<td>Elevated cholesterol</td>
<td></td>
</tr>
<tr>
<td>Factors associated with vascular disease *</td>
<td>Diabetes</td>
<td></td>
</tr>
<tr>
<td>Genetic factors (family history, gene mutations)</td>
<td>High homocysteine levels</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*HTN, hypercholesterolemia, CAD, stroke, smoker, obesity, diabetes

**How do the cholinesterase inhibitors work and what side effects can be expected?**\textsuperscript{[1]}

Cholinesterase inhibitors work by inhibiting the enzyme that breaks down acetylcholine, an important neurotransmitter for memory and cognition. Acetylcholine is decreased in patients with Alzheimer’s disease. There is no evidence to support that one cholinesterase inhibitor is more effective than the others.

Common adverse effects associated with this class of medications are nausea, vomiting and diarrhea. The incidence is greatest with oral Exelon (rivastigmine) however reduced with the patch. Anorexia, weight loss and dizziness are also common. Tremor is frequently reported with rivastigmine. Muscle cramps and insomnia are adverse effects associated with Aricept (donepezil). Decreased heart rate and fainting can occur. Urinary frequency or incontinence can worsen.

Cognex (tacrine) is no longer widely used due to frequent nausea/vomiting, the risk of liver toxicity and the need to be dosed four times a day.
Are generic Razadyne and Aricept just as good?

There is no literature comparing these specific brand drugs to their generic counterparts however there is information regarding generics in general. It is important to understand how generics come about. Developing a new drug is a very expensive endeavor therefore it is initially protected under a patent so that the company may earn money back on their efforts. After a designated number of years the patent expires and manufactures can apply to the FDA to sell generic versions. It is true that manufacturers of generics are not required to do extensive clinical trials however they have already been done by the brand company. Generic drugs must prove strict bioequivalence. One method is to measure the time it takes the drug to reach the bloodstream and concentration in the bloodstream in 24 to 36 healthy individuals. The generic must deliver the same amount of drug in the same amount of time as the brand to be approved. The manufacturers must also submit information on their manufacturing process to ensure good practices and inspections occur. An interesting fact is that brand name companies account for about 50% of generic drug production. Often a brand company will make its own generic.[4]

One question to ask is; how effective is a medication that a patient can’t afford? Generic substitutions can increase access and compliance and therefore the desired effect. One analysis evaluated claims data using medication possession ratio (MPR) to show that reduced cost has an effect on adherence. Greater adherence was found in patients receiving generic versus brand medications for hypercholesterolemia and hypertension. However, adherence rates for seizure disorders were low in both the brand and generic groups and adherence rates for hypothyroidism were very high regardless of brand or generic use. General conclusion is that use of generic medications can improve patient compliance.[5]

Some medications have too much variability and switching between brand and generics are not recommended. These include narrow therapeutic drugs such as Synthroid and Coumadin. However, most drugs have acceptable generics that offer the same safety and efficacy at a much reduced price.

How does Namenda work and what side effects are expected?[1]

Namenda (memantine) is an NMDA receptor antagonist. The NMDA receptor is the site for glutamate, an excitatory neurotransmitter, binding. Excessive glutamate binding leads to excessive levels of intra-neuronal calcium and ultimately neuronal damage.

Namenda is generally well tolerated however dizziness, confusion, headache, hallucinations, constipation and insomnia may occur.

When should we start treatment for dementia?

It is not clearly defined as when to initiate therapy.

Studies evaluating cholinesterase inhibitors in mild cognitive impairment have not shown improvement and therefore are not recommended in this situation. After diagnosis of Alzheimer’s disease, early use of cholinesterase inhibitors have shown benefit and are therefore recommended. [6]
When should we STOP treatment for dementia?

Also, not clearly defined. However…


- “Add-on therapy or considering memantine monotherapy should be instigated in patients with moderate disease when no stabilization or reduction in the rate of cognitive and functional decline is observed during ChEI monotherapy despite dose optimization and switching strategies.”

- “If a patient deteriorates to the point that there is dependency in all basic activities of daily living, or in the opinion of family members and the physician, meaningful social interactions and quality of life benefits are no longer possible, pharmacologic treatment should be withdrawn.”

- “Deterioration in cognition, function, or behavior during withdrawal may indicate a continuing response and may suggest the agent should be continued.”

The following is an abstract from the Journal of Palliative Care Medicine describing results of a survey to medical directors on when Alzheimer’s medications are discontinued.


**Background:** Cholinesterase inhibitors and N-methyl-D-aspartic acid (NMDA) receptor antagonists are Food and Drug Administration (FDA) approved for the treatment of moderate to severe Alzheimer's disease. As dementia progresses to the end stage and patients become hospice-eligible, clinicians consider whether or not to continue these therapies without the benefit of scientific evidence. We sought to describe hospice medical directors practice patterns and experiences in the use and discontinuation of cholinesterase inhibitors and NMDA receptor antagonists in hospice patients that meet the Medicare hospice criteria for dementia.

**Study Design:** Mail survey of hospice medical directors from a random sample from the National Hospice and Palliative Care Organization.

**Results:** Of the 413 eligible participants, 152 completed surveys were returned, yielding a response rate of 37%. Of the respondents, 75% and 33% reported that at least 20% of their patients were taking a cholinesterase inhibitor or memantine, respectively, at the time of hospice admission. The majority of respondents do not consider these therapies effective in persons with end-stage dementia, however, a subset believe that these medications improved patient outcomes including stabilization of cognition (22%), decrease in challenging behaviors (28%), and maintenance of patient function (22%) as well as caregiver outcomes namely reduced caregiver burden (20%) and improved caregiver quality of life (20%). While 80% of respondents recommended discontinuing these therapies to families at the time of hospice enrollment, 72% of respondents reported that families experienced difficulty stopping these therapies. A subset of respondents observed accelerated cognitive (30%) and functional decline (26%) or emergence of challenging behaviors (32%) with medication discontinuation.

**Conclusions:** The findings from this survey indicate that cholinesterase inhibitors and/or NMDA receptor antagonists are prescribed for a subset of patients with advanced dementia and that a proportion of hospice medical directors report clinical benefit from the ongoing use of these agents. In addition, physician preferences for discontinuing these therapies are frequently at odds with the wishes of family members. Prospective studies are needed to evaluate the clinical impact of the discontinuation of these therapies on patient and caregiver outcomes.
Can combinations of medications be used? → YES

A study by Tariot et al[7] compared adding memantine versus placebo to patient’s already receiving donepezil. This randomized, double blind study evaluated 404 patients with moderate to severe dementia over 24 weeks. The active group received memantine dose titration starting with 5mg daily and increased to 20mg daily. Multiple outcomes were used and evaluated cognition, activities of daily living, global outcome, behavior and tolerability. All outcomes were positive for memantine versus placebo. Treatment discontinuation rates were 7.4% versus 12.4% in the placebo and memantine arm, respectively.

Is gingko effective? → NO

The Gingko Evaluation of Memory (GEM) study confirmed what previous studies have found, that gingko biloba is ineffective in reducing the development of dementia. They enrolled 3,069 individuals aged 75 or older with normal cognition or mild impairment. The dose of gingko used was 120mg twice daily and was compared to placebo. Individuals were followed for an average of 6 years. The incidence of dementia diagnosis was not significantly different in the gingko versus placebo group (277 versus 246 in gingko and placebo, respectively p=0.21).[8]

What role do antipsychotics play for behavioral issues associated with dementia?

Antipsychotics are not approved by the FDA for treatment of behavioral issues in patients with dementia.

[In fact in 2005 the FDA mandated manufacturers of atypical antipsychotics to include a warning about increased death among elderly patients with dementia due to a 2 fold higher mortality rate associated with the class versus placebo.]

Other adverse effects include somnolence, gait changes, extrapyramidal effects, hyperglycemia and weight gain. In general, risk of adverse effects outweighs the benefits.[2]

It seems that prescribers are listening to the FDA. A study that looked at the rates of atypical antipsychotic use in patients over 65 years old and those with dementia found a decrease after the FDA warning was issued. Specifically, rates fell 2% overall and 19% in patients with dementia the following year.[9]

- However, this seems to indicate a substantial number of patients with dementia are still inappropriately prescribed antipsychotics.

Do any other medications have an impact?

Vascular risk factors seem to correlate with increased incidence of dementia. A review by Shah et al[10] evaluated the impact of anti-hypertensives on dementia. The analysis found a significant relationship between use of anti-hypertensives, specifically angiotensin converting enzyme inhibitors and diuretics, and a reduced rate of dementia. See attached table of studies.
Table I. Studies of the relationship between use of antihypertensive agents and the incidence and/or progression of dementia.

<table>
<thead>
<tr>
<th>Authors/Design*</th>
<th>Quality Score</th>
<th>Population</th>
<th>Age</th>
<th>Drug (Drug Class)</th>
<th>Duration of Follow-Up</th>
<th>Effect on Incidence/Progression of Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer’s dementia (AD)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Ohnue et al.19</td>
<td>5/6</td>
<td>Mild to moderate AD</td>
<td>≥65 y</td>
<td>Perindopril or captopril (brain-penetrating ACE inhibitor); enalapril or irinapril (non-brain-penetrating ACE inhibitor); nifedipine or nivalidipine (CCB)</td>
<td>1 y</td>
<td>Decrease in progression beyond decrease in BP with perindopril or captopril; no decrease in progression with other agents</td>
</tr>
<tr>
<td>Yasir et al.20</td>
<td>3/6</td>
<td>Incident dementia</td>
<td>&gt;60 y</td>
<td>CCBs</td>
<td>Mean 11 y</td>
<td>No decrease in incidence</td>
</tr>
<tr>
<td>Hajari et al.21</td>
<td>2/6</td>
<td>Hypertension (84% of population, 54% treated); AD and VaD</td>
<td>Mean 77 y</td>
<td>ACE inhibitors, ARBs, CCBs, β-blockers, diuretics, β-blockers, clonidine, others</td>
<td>Mean 2 y</td>
<td>Overall decrease in progression</td>
</tr>
<tr>
<td>Khachaturian et al.22</td>
<td>5/6</td>
<td>Incident AD (mean 74 y)</td>
<td>≥65 y</td>
<td>ACE inhibitors, β-blockers, CCBs, diuretics</td>
<td>1.5 y</td>
<td>Overall decrease in incidence beyond decrease in BP; decreased incidence with potassium-sparing diuretics but not with other drug classes</td>
</tr>
<tr>
<td>Qiu et al.23</td>
<td>2/6</td>
<td>No AD at baseline</td>
<td>≥75 y</td>
<td>Antihypertensives overall</td>
<td>9 y</td>
<td>Overall decrease in incidence</td>
</tr>
<tr>
<td>Hanon et al.24</td>
<td>2/6</td>
<td>Memory loss</td>
<td>≥65 y</td>
<td>CCBs, β-blockers, diuretics</td>
<td>–</td>
<td>Overall decreases in incidence of AD and VaD beyond decrease in BP; incidence of AD decreased beyond decrease in BP with CCBs; no decrease in incidence or progression of AD or VaD with other classes</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Authors/Design*</th>
<th>Quality Score</th>
<th>Population</th>
<th>Age</th>
<th>Drug (Drug Class)</th>
<th>Duration of Follow-Up</th>
<th>Effect on Incidence/Progression of Dementia</th>
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<tbody>
<tr>
<td>Vascular dementia (VaD)</td>
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<tr>
<td>Hannon et al.24 (see AD)</td>
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<tr>
<td>Tzourio et al.25</td>
<td>6/8</td>
<td>Previous stroke or TIA</td>
<td>Mean 64 y</td>
<td>Perindopril (ACE inhibitor) with possible add-on indapamide (diuretic)</td>
<td>4 y</td>
<td>Decreased incidence of VaD; no decrease in incidence of unspecified dementia</td>
</tr>
<tr>
<td>Pannoni et al.26</td>
<td>4/8</td>
<td>Subcortical VaD</td>
<td>45–85 y</td>
<td>Nimodipine (CCB)</td>
<td>6 mo</td>
<td>No decrease in progression</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Authors/Design*</th>
<th>Quality Score</th>
<th>Population</th>
<th>Age</th>
<th>Drug (Drug Class)</th>
<th>Duration of Follow-Up</th>
<th>Effect on Incidence/Progression of Dementia</th>
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<tbody>
<tr>
<td>Unspecified dementia</td>
<td></td>
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<tr>
<td>Tzourio et al.27 (see VaD)</td>
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<tr>
<td>Guo et al.27</td>
<td>4/6</td>
<td>Hypertension at baseline</td>
<td>≥75 y</td>
<td>Diuretics (mainly), CCBs, β-blockers</td>
<td>Mean 36.7 mo</td>
<td>Overall decrease in incidence; incidence and progression decreased with diuretics; no decrease in incidence with other classes</td>
</tr>
<tr>
<td>Fornette et al.28</td>
<td>6/8</td>
<td>No dementia at baseline; systolic BP 160–219 mm Hg, diastolic BP &lt;95 mm Hg</td>
<td>≥60 y</td>
<td>Nitrendipine (CCB), with possible add-on enalapril (ACE inhibitor) and/or HCTZ (diuretic)</td>
<td>Median 3.9 y</td>
<td>Decrease in incidence</td>
</tr>
<tr>
<td>Skoog et al.29</td>
<td>5/8</td>
<td>No dementia at baseline</td>
<td>≥70 y</td>
<td>Candesartan (ARB)</td>
<td>Mean 3–5 y</td>
<td>No decrease in incidence</td>
</tr>
<tr>
<td>Peters et al.30</td>
<td>6/8</td>
<td>Hypertension at baseline</td>
<td>≥80 y</td>
<td>Indapamide (diuretic) with possible add-on perindopril (ACE inhibitor)</td>
<td>Mean 2.2 y</td>
<td>No decrease in incidence</td>
</tr>
</tbody>
</table>

*Authors/Design:
- R, PC, prospective cohort study
- Cohort study
- Longitudinal analysis of a retrospective cohort study
- Population-based cohort study
- Community-based cohort study
- Cross-sectional study

*Quality Score:
- 5/6: Evidence level A
- 4/6: Evidence level B
- 3/6: Evidence level C

*Drug (Drug Class):
- ACE: Angiotensin-Converting Enzyme
- ARB: Angiotensin Receptor Blocker
- CCB: Calcium Channel Blocker
- Diuretic
- β-blocker
- Others
The Cochrane group [11] did a review to determine if statins affect the incidence of dementia. The analysis consisted of data from two large studies, HPS 2002 and PROSPER 2002. Both were designed to evaluate placebo versus statin, pravastatin in PROSPER and simvastatin in HPS. The two studies found no decrease in incidence of dementia or rate of cognition decline. See charts below.

### Analysis 1.1. Comparison 1 Incidence of dementia, Outcome 1 Number of cases of dementia.

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Odds Ratio</th>
<th>Weight</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>M-H/Fixed</td>
<td></td>
<td>M-H/Fixed</td>
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<tr>
<td>HPS 2002</td>
<td>317/0269</td>
<td>317/0267</td>
<td></td>
<td>100.0%</td>
<td>1.00</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>10269</td>
<td>10267</td>
<td></td>
<td>100.0%</td>
<td>1.00 [0.61, 1.65]</td>
</tr>
</tbody>
</table>

Total events: 31 (Experimental), 31 (Control)
Heterogeneity not applicable
Test for overall effect: Z = 0.00 (P = 1.0)

### Analysis 2.1. Comparison 2 Cognitive change from baseline, Outcome 1 Change in MMSE.

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Statin</th>
<th>Placebo</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
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<tr>
<td></td>
<td>N</td>
<td>N</td>
<td>(SE)</td>
<td></td>
<td>(SE)</td>
</tr>
<tr>
<td>PROSPER</td>
<td>2891</td>
<td>2891</td>
<td>0.06 (0.08)</td>
<td>100.0%</td>
<td>0.06 [-0.04, 0.16]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td>100.0%</td>
<td>0.06 [-0.04, 0.16]</td>
</tr>
</tbody>
</table>

Heterogeneity not applicable
Test for overall effect: Z = 1.20 (P = 0.23)

What medications can worsen dementia?

**Anticholinergics**
- Antihistamines (i.e., diphenhydramine, hydroxyzine)
- Overactive bladder drugs (i.e., tolterodine, oxybutynin)
- Tricyclic antidepressants (i.e., imipramine, nortriptyline)
### Summary of Advantages/Disadvantages of treatments options

<table>
<thead>
<tr>
<th>Drug</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
</table>
| Cognex (tacrine)| - Requires QID dosing  
- Frequent N/V  
- Risk of liver toxicity |                                                                 |
| Aricept (donepezil)| - Oral disintegrating tablet formulation  
- Generic available (NEW)  
- Indicated for mild, moderate and severe dementia | - Associated with nightmares/ insomnia |
| Razadyne (galantamine)| - Generic available | - Associated with tremors  
- No generic yet |
| Exelon (rivastigmine)| - Patch formulation  
- Most information for Lewy Body/Parkinson’s dementia | - Frequent N/V (decreased with patch) |
| Namenda (memantine)| - Not very effective as monotherapy | - Offers benefit as add on therapy in moderate to severe dementia  
- Well tolerated |
| Gingko          |                                                                         | - Ineffective                                       |
| Antipsychotics  | - May improve behavior                                                   | - Increased risk of death  
- Many side effects |

### References

Answer Key

1. A
2. C
3. C
4. B
5. B
6. B
7. D