# The Primary Care Guide To The Use Of Statins As A Preventive Intervention For Dementia

## 1. Overview:

The primary care physician may be queried about the role of dyslipidemia and statin therapy in the pathogenesis or prevention of dementia. Elevated cholesterol and triglyceride levels are significant health problems in middle-aged and older individuals. Reduction of low density lipoprotein cholesterol by 25% to 40% will diminish the frequency of coronary events by 20 to 40%. Longitudinal studies demonstrate as much as 24% reductions in cardiovascular events after long-term treatment over 5 to 6 years. Elevated cholesterol and triglyceride levels are integral parts of the metabolic syndrome which afflicts approximately 25% of older Americans (5).

## 2. Mechanisms of Action

The potential protective mechanisms of statin use for cognition include: 1) reduction of damage to large caliber and small caliber vasculature, 2) reduction of inflammation in the brain, and 3) retardation of amyloid deposits. Despite these proposed mechanisms, the overall data on protective effect of statin usage remains unclear (11). A review of nine recent studies on the impact of statin therapy in cognition and dementia provided mixed results (11). A meta-analysis of 7 studies with 13,920 subjects demonstrated reduction of dementia (-30%) and Alzheimer's disease (-20%) with treatment; however, this effect "signal" was lost in the study's "noise". A variety of studies using multiple research techniques including longitudinal studies, nested case matching, and other statistical methods provide conflicting data. The CSF beta amyloid levels in older individuals do not appear affected by statin usage; however, plasma beta amyloid 42 levels in non-demented persons over age 75 appear slightly diminished in subjects receiving long-term statin therapy (12). The clinical significance of these scientific observations remains unclear. Treatment with Atorvastin may enhance cognitive function in persons with mild or moderate dementia (17).

Cell culture and rodent studies indicate that statin therapy may reduce the deposition of amyloid or impede aggregation of amyloid fibrils. No benefit is presently identified against the hyper-phosphorylation of tau or other markers for the production of neurofibrillary tangles. Neuropathological studies in humans who receive statin therapy prior to death indicate a strong linear association between increased LDL cholesterol levels and increased numbers of senile plaque or neurofibrillary tangles (13).

## 3. Clinical Recommendations

The global vascular benefit of statin therapy is supported by most research. Treatment of individuals with abnormal lipid levels is recommended, regardless of the patient's age. The prophylactic use of statins to prevent dementia in persons with normal lipids is not recommended because the risk-benefit ratio does not support the use of these expensive agents (15). The treatment of dyslipidemia in the setting of metabolic syndrome may provide greater benefit, as this intervention may assist with the reduction of intrinsic, brain inflammatory responses. No specific type of medication or diet has been demonstrated as potentially more beneficial for possible cognitive protection. The

beneficial effect of statin therapy in mild to moderate dementia also remains controversial (11), (14), (15).

Statin therapy may produce numerous risks and side effects including mylagias and hepatotoxicity with some agents (16). Long-term compliance with diet and medication is a therapeutic challenge in the primary care setting. Longitudinal studies suggest that about 50% of patients comply with long-term statin therapy. Sufficient data exists about brain protection to provide the additional encouragement that long-term lipid management may significantly reduce the risk for cerebrovascular events and cognitive decline in later life. Strict adherence to lipid management may provide a significant beneficial, cognitive effect to those individuals with dyslipidemias (18) ***(For more information on compliance, See 2514.1).*** Dietary restriction of trans-fat may further reduce the risk for dementia (click here for additional information _____).

**Recommendations**

1. Check lipid profiles in older persons.
2. Promote diet and weight control as lipid lowering interventions.
3. Treat dyslipidemia when identified in patients.
4. Use the concept of brain protection to encourage compliance with statin medications.
5. Do not use statins as a "preventive" measure against dementia in persons with normal lipid profiles.
6. Use "brain protection" as another argument to promote medication and dietary compliance in patients with hyperlipidemia.

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