

Determining Dementia Risk: What Factors to Consider?

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Who gets dementia?

Age is the biggest risk factor for the development of dementia.¹ The estimated annual incidence of Alzheimer's disease is 1% in individuals aged 70 to 74 years and steadily increases with age. The incidence of dementia in those over 85 years of age is 8.5%.

Alzheimer's is the most common form of dementia, followed by vascular, mixed, Lewy body and frontotemporal dementia. First

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degree relatives of patients with Alzheimer's or vascular dementia have a 10% to 30% increased lifetime risk of developing dementia.² This risk is highest the earlier the age of onset was in the afflicted individual.

Mild cognitive impairment (MCI) primarily presents with a memory problem in patients with preserved general cognitive function, while activities of daily living are not significantly compromised. The memory disturbance can be objectively confirmed. Scores on the mini mental status exam will typically be in the 27 to 29 range, with points lost on the three-item recall. This is a high-risk group with an approximate 15% chance of deterioration to dementia each year.

Self-reported memory loss is also typical of normal aging. With normal aging, the rate of information processing and the rate of acquisition performance (learning) slows, but information is not

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Table 1

Stroke prevention strategies

- Control systolic hypertension in the elderly (target < 140/90 mmHg)
- Control hypertension in diabetes (target < 130/80 mmHg)
- Smoking cessation
- Optimize lipids in patients with cardiovascular disease (secondary prevention)
- Anticoagulation for atrial fibrillation in those over age 75 (relative risk reduction = 68%)

forgotten once it is learned. The early retrieval of new information declines, but delayed recall is preserved.

How do hypertension and cerebrovascular disease affect dementia?

Hypertension is associated with an increased risk of both Alzheimer's disease and vascular dementia.^{3,4}

The Syst-Eur Dementia trial, published in 2002, is the only randomized controlled trial (RCT) on hypertension treatment and dementia prevention.⁵ It included over 2,400 patients older than 65 years of age with systolic BP between 160 mmHg to 219 mmHg and diastolic BP below 95 mmHg at entry. It demonstrated that the treatment of BP to a goal of < 140/90 mmHg resulted in a 55% relative risk reduction in the diagnosis of dementia (Alzheimer's and vascular) in the active treatment group over the course of the four-year study period.



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The Perindopril Protection Against Recurrent Stroke Study (PROGRESS) trial, an RCT that included 6,100 patients with a prior history of stroke or transient ischemic attack demonstrated a 34% relative risk reduction for dementia in participants treated with perindopril plus indapamide, regardless if they were hypertensive or normotensive at entry into the study.⁶

The NUNS study revealed that the hallmark pathologic findings of plaques and neurofibrillary tangles that characterize Alzheimer's dementia, when present, were much more likely to have expressed clinical dementia in the lives of nuns who also had pathologic changes of vascular disease (*i.e.*, lacunar infarcts), identified at the time of brain autopsy.⁷ Physicians should consider stroke prevention strategies as parallel with dementia prevention strategies (Table 1).

Does inflammation play a role in dementia?

There is accumulating evidence that statins may reduce the risk of dementia via their anti-inflammatory effects. Statins have been demonstrated *in vitro* to suppress the production of amyloid peptides Abeta40 and Abeta42, which are the primary building blocks for the plaques and neurofibrillary tangles that are characteristically found in Alzheimer brains.⁸

Similarly, traditional nonsteroidal anti-inflammatory drugs (NSAIDs) may also mediate reduced dementia risk through their anti-inflammatory effects. Taking NSAIDs regularly for more than two years seems to be the critical length of time for reducing dementia risk.^{9,10} Ibuprofen, at a dosage of 200 mg/day, seems to be the most promising NSAID in this regard. Acetylsalicylic acid (ASA) appears to offer less protection. The cyclooxygenase-2 (Cox-2) inhibitors, which are prothrombotic, have demonstrated no benefit toward reducing dementia risk.

Are postmenopausal hormones protective against dementia?

Up until the release of the Women's Health Initiative (WHI) in July 2002, prior observational data suggested the possibility of a protective effect on cardiovascular function and cognitive performance in women undergoing postmenopausal hormone replacement therapy (HRT). However, the WHI revealed an increased risk of stroke and coronary artery disease in women taking HRT for more than five years. The WHI Memory Study also demonstrated a trend toward an increased risk of MCI and dementia in those treated with long-term HRT. The protective effects of HRT against osteoporosis and reduced bowel cancer risk are superseded by the increased risk of cardiovascular disease, stroke and dementia. Now, postmenopausal HRT is only recommended for symptom control and preferably for less than five years.

Does leading a healthy lifestyle reduce your risk of developing dementia?

Oxidative stress may be important in the pathogenesis of Alzheimer's disease. Two large, prospective cohort studies have shown an association between the higher dietary intake of antioxidants, especially vitamin E, and a lower risk of Alzheimer's disease. It is unclear whether antioxidant supplements have a beneficial role in this instance. The Alzheimer's Disease Cooperative Study is an RCT presently underway to determine whether vitamin E and donepezil may have a role to play in slowing the conversion of MCI to dementia.


Available epidemiologic data shows conflicting results regarding the role of diet and exercise in dementia prevention. However, engaging in certain types of cognitive leisure activities, including reading, playing board games and playing a musical instrument, may have

some protective effect against dementia. Evidence increasingly suggests that light to moderate drinking may also be protective.

It is possible that significant head trauma may increase the risk for subsequent development of demen-

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tia. Untreated or incompletely treated depression may also be associated with an increased future risk of dementia. We know that depression also adds to the risk of subsequent cardiovascular disease.

Aside from the two irreversible risk factors of age and family history, there are several other risks for which implementing treatment measures may have some benefit in reducing the risk of developing dementia. 

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