



**An Australian Government Initiative**

# **DEMENTIA RISK REDUCTION RESEARCH**

## **2008**

**Research relevant to Mind your Mind**

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Alzheimer's Australia Vic**



**Alzheimer's  
Australia**  
Living with dementia



**DCRC**  
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Research Centres

## Acknowledgements and Disclaimers

This paper was prepared as part of Alzheimer's Australia Vic's involvement in the Dementia Collaborative Research Centre Number 2: Prevention, Early Intervention and Risk Reduction.

The Dementia Collaborative Research Centres are an Australian Government funded initiative established to advance Australian research into dementia and the translation of research into clinical practice. The three Centres each focus on a different area of dementia research:

- Assessment and better care outcomes
- Prevention, early intervention and risk reduction
- Consumers, carers and social research

Visit the Dementia Collaborative Research Centres website at [www.dementia.unsw.edu.au](http://www.dementia.unsw.edu.au) for further information about the people involved and the research activities.

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## DEMENTIA RISK REDUCTION RESEARCH 2008

### Journal articles relevant to Alzheimer's Australia's Mind your Mind® program

Compiled by Dr Maree Farrow, Research Fellow, Alzheimer's Australia Vic

This document includes summaries of research articles published in 2008 that describe or review research into risk factors, risk reduction or prevention of dementia. It is not intended to be a complete list of all research in the area, but instead concentrates on articles relevant to Mind your Mind, Alzheimer's Australia's dementia risk reduction community education program.

You can click on a title in the table of contents to go straight to that article. *Section One* includes review articles, papers that analyse the results of past research to address an issue, and *Section Two* includes papers describing individual research studies.

For each article, under the heading *Main Message*, the main points raised or main findings of the research are summarised. Under the heading *Note*, any issues to consider in interpreting the findings are noted. This is only included where relevant. Under the heading *Abstract*, is the abstract from the original article, i.e. the authors' summary of their paper.

The icons to the left of each article represent the Mind your Mind signposts that the research addresses. The seven signposts and their icons are:



Mind your Brain



Mind your Body



Mind your Diet



Mind your Health Checks



Mind your Social Life



Mind your Habits



Mind your Head

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## **SECTION ONE – REVIEWS**

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### **Smoking increases risk of Alzheimer's disease**

**Date published:** December 2008

#### **Main Message**

This review of smoking studies found a significantly increased risk of Alzheimer's disease with current smoking and a likely increased risk of vascular dementia, dementia unspecified and cognitive decline. Consistent with previous reviews, these findings demonstrate that current smoking increases risk of Alzheimer's disease.

#### **Abstract**

**BACKGROUND:** Nicotine may aid reaction time, learning and memory, but smoking increases cardiovascular risk. Cardiovascular risk factors have been linked to increased risk of dementia. A previous meta-analysis found that current smokers were at higher risk of subsequent dementia, Alzheimer's disease, vascular dementia and cognitive decline.

**METHODS:** In order to update and examine this further a systematic review and meta-analysis was carried out using different search and inclusion criteria, database selection and more recent publications. Both reviews were restricted to those aged 65 and over.

**RESULTS:** The review reported here found a significantly increased risk of Alzheimer's disease with current smoking and a likely but not significantly increased risk of vascular dementia, dementia unspecified and cognitive decline. Neither review found clear relationships with former smoking.

**CONCLUSION:** Current smoking increases risk of Alzheimer's disease and may increase risk of other dementias. This reinforces need for smoking cessation, particularly aged 65 and over. Nicotine alone needs further investigation.

#### **Reference**

Peters R, et al. Smoking, dementia and cognitive decline in the elderly, a systematic review. *BMC Geriatrics*, 2008, December 23, 8:36, doi: 10.1186/1471-2318-8-36.





## Type 2 diabetes is associated with increased risk of dementia

**Date published:** November 2008

### Main Message

This review concludes that type 2 diabetes is associated with increased risk for Alzheimer's disease and vascular dementia, but the underlying mechanisms behind this association remain to be clearly determined.

### Abstract

**INTRODUCTION:** The prevalence of type 2 diabetes and dementia are set to rise inexorably over the next 30-40 years. There are now substantial data to suggest that type 2 diabetes is associated with an increased risk of dementia.

**SOURCES OF DATA:** This is a narrative review using data from individual studies and review articles known to the authors. A Medline search was also undertaken and reference lists were reviewed to identify additional relevant studies.

**AREAS OF AGREEMENT:** Type 2 diabetes is associated with an increased risk of both Alzheimer's and Vascular dementia, although the reality is that many affected individuals have mixed forms of dementia.

**AREAS OF CONTROVERSY:** The mechanisms underpinning this association remain to be clearly delineated. Type 2 diabetes is a complex disorder and so it is likely that multiple different, synergistic processes may interact to promote cognitive decrements.

**GROWING POINTS:** Recent data suggest that glucocorticoids excess and elevated inflammatory markers may also have a role in the aetiology of diabetes-related cognitive impairment.

**AREAS TIMELY FOR DEVELOPING RESEARCH:** Large-scale, prospective epidemiological studies are now required to accurately delineate the pathogenesis of cognitive impairment in people with type 2 diabetes. These are underway and randomized trials of diabetes-specific interventions are also starting to include cognitive function as an outcome measure.

### Reference

Strachan MW, et al. The relationship between type 2 diabetes and dementia. *British Medical Bulletin*, 2008, 88:131-146.



## High blood pressure and cognitive function

*Date published: November 2008*

### Main Message

Hypertension (high blood pressure) is associated with cerebrovascular disease, which is in turn associated with dementia. It is the most important modifiable risk factor for stroke, which is a recognised cause of vascular dementia. Increasing clinical evidence suggests a close relationship between the reduction of elevated blood pressure and countering of both vascular dementia and Alzheimer's disease. Antihypertensive treatment probably prevents cognitive function alterations and the development of dementia.

### Abstract

Arterial hypertension, cerebrovascular disease, and dementia are related pathologies. This paper has reviewed comparatively the incidence of arterial hypertension and adult-onset dementia disorders. Hypertension is associated with cerebrovascular disease, which is in turn associated with dementia. It is the most important modifiable risk factor for stroke, which is a recognized cause of vascular dementia. In terms of pathophysiology of hypertensive brain damage, several hypotheses were developed, such as that vascular alterations induced by hypertension can induce lacunar or cortical infarcts and leucoaraiosis, that hypertension is responsible for cerebrovascular disease and acts into the contest of a pre-existing subclinic Alzheimer's disease (AD), that hypertension determines neurobiologic alterations (such as beta-amyloid accumulation) resulting in neuropathologic damage, and that aging and cerebrovascular risk factors act together to cause cerebral capillary degeneration, mitochondrial disruption, reduced glucose oxidation, and reduced ATP synthesis. The consequence of these alterations are neuronal death and dementia. Macroscopic results of these mechanisms are the so-called white matter lesions (WML), the significance of which is analyzed. Increasing clinical evidence suggests a close relationship between the reduction of elevated blood pressure and countering of both vascular dementia and AD. Antihypertensive treatment probably influences cognitive performances and prevents cognitive function alterations and the development of dementia. It is therefore important to evaluate as soon as possible cognitive functions of hypertensive patients.

### Reference

Paglieri C, et al. Hypertension and cognitive function. *Clinical and Experimental Hypertension*, 2008, 30:701-710.



## Effects of blood pressure on dementia risk depend on age

**Date published:** November 2008

### Main Message

This review concludes that high blood pressure in midlife is associated with increased risk of both Alzheimer's disease (AD) and vascular dementia in later life, due to cerebrovascular changes from long standing high blood pressure. Low blood pressure in late-life is also associated with an increased risk of AD. A decline in blood pressure in later life may contribute to diminished cerebral perfusion and increased beta-amyloid accumulation.

### Abstract

Alzheimer's disease (AD) and vascular dementia (VaD) are important causes of cognitive decline in the elderly. As a result of the aging population, the incidence of dementia is expected to increase substantially over the coming decades. Many studies have identified that vascular risk factors are implicated in the pathogenesis of both AD and VaD. Longitudinal studies have suggested that high blood pressure in midlife is associated with a higher incidence of both AD and VaD in later life. The association appears weaker for hypertension in later life. Some studies also suggest that hypotension; especially low diastolic blood pressure in late-life is also associated with an increased risk of AD. Long-standing hypertension may lead to severe atherosclerosis and impaired cerebrovascular autoregulation. A decline in blood pressure in later life may contribute to diminished cerebral perfusion. The subsequent ischaemic state may lead to increased cerebral beta-amyloid accumulation.

### Reference

Kennelly SP, et al. Blood pressure and the risk for dementia: a double edged sword. *Ageing Research Reviews*, 2008. Published online 21 November 2008, doi:10.1016/j.arr.2008.11.001



## Healthy lifestyle and the prevention of dementia

*Date published: November 2008*

### Main Message

This review summarises the current understanding about risk and protective factors for dementia. Factors that have been associated with increased risk of developing dementia include high blood pressure, high body mass index and smoking. Having education and maintaining a Mediterranean diet, including vegetable, fruit and fish intake, have been linked to a lower incidence of dementia. The maintenance of a healthy lifestyle may represent the best option with regard to the prevention of dementia.

### Abstract

**OBJECTIVE:** Dementia is prevalent in older adults and the population is ageing. Many factors have been associated with dementia and anything that may aid the prevention of dementia is of importance.

**METHOD:** The literature in this area was evaluated and information relating to the various factors that may impact upon the prevention of dementia is presented below.

**RESULTS:** Factors that have been associated with a possible increased risk of developing dementia include high blood pressure, (at least in midlife), high body mass index, smoking and possibly diabetes although the evidence is mixed. There is currently no clear evidence with regard to cholesterol and metabolic syndrome although both may be implicated. Having education and maintaining a Mediterranean diet, including vegetable, fruit and fish intake, have been linked to a lower incidence of dementia as has low to moderate alcohol intake. Although care must be taken with the latter given the different characteristics of the studies reporting on alcohol and dementia.

**CONCLUSION:** It may be that risk and protective factors vary with age, however, in the absence of prophylactic treatment it seems likely that the maintenance of a healthy lifestyle may represent the best option with regard to the prevention of dementia.

### Reference

Peters R. The prevention of dementia. *International Journal of Geriatric Psychiatry*, 2008. Published Online: 21 November 2008, doi: 10.1002/gps.2153



## Folate supplements do not improve cognitive function

*Date published: October 2008*

### Main Message

This review found that the small number of studies which have been undertaken provide no consistent evidence either way that folic acid, with or without vitamin B12, has a beneficial effect on cognitive function of unselected healthy or cognitively impaired older people. However, long-term use may improve the cognitive function of healthy older people with high homocysteine levels. The findings suggest that folate supplements are only helpful for those with high homocysteine or folate deficiency.

### Note

This paper reviewed randomised controlled trials and found no consistent benefit of folate supplements, but there are some cohort studies that demonstrate reduced risk of dementia with higher folate intake. More research is needed.

### Abstract

**BACKGROUND:** Folate deficiency can result in congenital neural tube defects and megaloblastic anaemia. Low folate levels may be due to insufficient dietary intake or inefficient absorption, but impaired metabolic utilization also occurs. Because B12 deficiency can produce a similar anaemia to folate deficiency, there is a risk that folate supplementation can delay the diagnosis of B12 deficiency, which can cause irreversible neurological damage. Folic acid supplements may sometimes therefore include vitamin B12 supplements with simultaneous administration of vitamin B12. Lesser degrees of folate inadequacy are associated with high blood levels of the amino acid homocysteine which has been linked with the risk of arterial disease, dementia and Alzheimer's disease. There is therefore interest in whether dietary supplementation can improve cognitive function in the elderly. However, any apparent benefit from folic acid which was given in combination with B12 needs to be "corrected" for any effect of vitamin B12 alone. A separate Cochrane review of vitamin B12 and cognitive function has therefore been published.

**OBJECTIVES:** To examine the effects of folic acid supplementation, with or without vitamin B12, on elderly healthy or demented people, in preventing cognitive impairment or retarding its progress.

**SEARCH STRATEGY:** Trials were identified from a search of the Cochrane Dementia and Cognitive Improvement Group's Specialized Register on 10 October 2007 using the terms: folic acid, folate, vitamin B9, leucovorin, methyltetrahydrofolate, vitamin B12, cobalamin and cyanocobalamin. This Register contains references from all major health care databases and many ongoing trials databases. In addition MEDLINE, EMBASE, CINAHL, PsychINFO and LILACS were searched (years 2003-2007) for additional trials of folate with or without vitamin B12 on healthy elderly people.

**SELECTION CRITERIA:** All double-blind, placebo-controlled, randomized trials, in which supplements of folic acid with or without vitamin B12 were compared with placebo for elderly healthy people or people with any type of dementia or cognitive impairment.

**DATA COLLECTION AND ANALYSIS:** The reviewers independently applied the selection criteria and assessed study quality. One reviewer extracted and analysed the data. In comparing intervention with placebo, weighted mean differences and standardized mean difference or odds ratios were estimated.

**MAIN RESULTS:** Eight randomized controlled trials fulfilled the inclusion criteria for this review. Four trials enrolled healthy older people, and four recruited participants with mild to moderate cognitive impairment or dementia with or without diagnosed folate deficiency. Pooling the data was not possible owing to heterogeneity in sample selections, outcomes, trial duration, and dosage. Two studies involved a combination of folic acid and vitamin B12. There is no adequate evidence of benefit from folic acid supplementation with or without vitamin B12 on cognitive function and mood of unselected healthy elderly people. However, in one trial enrolling a selected group of healthy elderly people with high homocysteine levels, 800 mcg/day folic acid supplementation over three years was associated with significant benefit in terms of global functioning (WMD 0.05, 95% CI 0.004 to 0.096,  $P = 0.033$ ); memory storage (WMD 0.14, 95% CI 0.04 to 0.24,  $P = 0.006$ ) and information-processing speed (WMD 0.09, 95% CI 0.02 to 0.16,  $P = 0.016$ ). Four trials involved people with cognitive impairment. In one pilot trial enrolling people with Alzheimer's disease, the overall response to cholinesterase inhibitors significantly improved with folic acid at a dose of 1mg/day (odds ratio: 4.06, 95% CI 1.22 to 13.53;  $P = 0.02$ ) and there was a significant improvement in scores on the Instrumental Activities of Daily Living and the Social Behaviour subscale of the Nurse's Observation Scale for Geriatric Patients (WMD 4.01, 95% CI 0.50 to 7.52,  $P = 0.02$ ). Other trials involving people with cognitive impairment did not show any benefit in measures of cognitive function from folic acid, with or without vitamin B12. Folic acid plus vitamin B12 was effective in reducing serum homocysteine concentrations (WMD -5.90, 95% CI -8.43 to -3.37,  $P < 0.00001$ ). Folic acid was well tolerated and no adverse effects were reported.

**AUTHORS' CONCLUSIONS:** The small number of studies which have been done provide no consistent evidence either way that folic acid, with or without vitamin B12, has a beneficial effect on cognitive function of unselected healthy or cognitively impaired older people. In a preliminary study, folic acid was associated with improvement in the response of people with Alzheimer's disease to cholinesterase inhibitors. In another, long-term use appeared to improve the cognitive function of healthy older people with high homocysteine levels. More studies are needed on this important issue.

## Reference

Malouf R, Grimley Evans J. Folic acid with or without vitamin B12 for the prevention and treatment of healthy elderly and demented people. *Cochrane Database of Systematic Reviews*, 2008, Issue 4, Art. No. CD004514. DOI: 10.1002/14651858.CD004514.pub2



## Alcohol in small amounts reduces dementia risk

**Date published:** September 2008

### Main Message

This meta-analysis of 23 studies concluded that small amounts of alcohol are associated with a 37% reduced risk of dementia and a 43% reduced risk of Alzheimer's disease, suggesting that limited alcohol intake in earlier adult life may be protective against incident dementia later.

### Abstract

**BACKGROUND:** dementia and cognitive decline have been linked to cardiovascular risk. Alcohol has known negative effects in large quantities but may be protective for the cardiovascular system in smaller amounts. Effect of alcohol intake may be greater in the elderly and may impact on cognition.

**METHODS:** to evaluate the evidence for any relationship between incident cognitive decline or dementia in the elderly and alcohol consumption, a systematic review and meta-analyses were carried out. Criteria for inclusion were longitudinal studies of subjects aged  $\geq 65$ , with primary outcomes of incident dementia/cognitive decline.

**RESULTS:** 23 studies were identified (20 epidemiological cohort, three retrospective matched case-control nested in a cohort). Meta-analyses suggest that small amounts of alcohol may be protective against dementia (random effects model, risk ratio [RR] 0.63; 95% CI 0.53-0.75) and Alzheimer's disease (RR 0.57; 0.44-0.74) but not for vascular dementia (RR 0.82; 0.50-1.35) or cognitive decline (RR 0.89; 0.67-1.17) However, studies varied, with differing lengths of follow up, measurement of alcohol intake, inclusion of true abstainers and assessment of potential confounders.

**CONCLUSIONS:** Because of the heterogeneity in the data these findings should be interpreted with caution. However, there is some evidence to suggest that limited alcohol intake in earlier adult life may be protective against incident dementia later.

### Reference

Peters R, et al. Alcohol, dementia and cognitive decline in the elderly: a systematic review. *Age and Ageing*, 2008, 37:505-512.



## The role of diet in the risk for Alzheimer's disease

**Date published:** August 2008

### Main Message

This review concludes that a diet that helps reduce obesity, high blood pressure, high cholesterol and insulin resistance may also reduce the risk of Alzheimer's disease. This may be especially important for people at increased risk, such as those with a family history or features of metabolic syndrome.

### Abstract

Since Alzheimer's disease (AD) has no cure or preventive treatment, an urgent need exists to find a means of preventing, delaying the onset, or reversing the course of the disease. Clinical and epidemiological evidence suggests that lifestyle factors, especially nutrition, may be crucial in controlling AD. Unhealthy lifestyle choices lead to an increasing incidence of obesity, dyslipidemia and hypertension--components of the metabolic syndrome. These disorders can also be linked to AD. Recent research supports the hypothesis that calorie intake, among other non-genetic factors, can influence the risk of clinical dementia. In animal studies, high calorie intake in the form of saturated fat promoted AD-type amyloidosis, while calorie restriction via reduced carbohydrate intake prevented it. Pending further study, it is prudent to recommend to those at risk for AD--e.g. with a family history or features of metabolic syndrome, such as obesity, insulin insensitivity, etc.--to avoid foods and beverages with added sugars; to eat whole, unrefined foods with natural fats, especially fish, nuts and seeds, olives and olive oil; and to minimize foods that disrupt insulin and blood sugar balance.

### Reference

Pasinetti GM, Eberstein JA. Metabolic syndrome and the role of dietary lifestyles in Alzheimer's disease. *Journal of Neurochemistry*, 2008, 106:1503-1514.



## Obesity increases dementia risk

*Date published: May 2008*

### Main Message

This meta-analysis of 10 studies found that compared to those of normal weight, those who were underweight had a 36% increased risk of any dementia and those who were obese had a 42% increased risk of any dementia. Obesity was associated with an 80% increased risk of Alzheimer's and 73% increased risk of vascular dementia, and the associations were stronger for obesity measured at a younger age.

### Abstract

While dementia affects 6-10% of persons 65 years or older, industrialized countries have witnessed an alarming rise in obesity. However, obesity's influence on dementia remains poorly understood. We conducted a systematic review and meta-analysis. PUBMED search (1995-2007) resulted in 10 relevant prospective cohort studies of older adults (40-80 years at baseline) with end points being dementia and predictors including adiposity measures, such as body mass index (BMI) and waist circumference (WC). There was a significant U-shaped association between BMI and dementia ( $P = 0.034$ ), with dementia risk increased for obesity and underweight. Pooled odds ratios (OR) and 95% confidence intervals (CI) for underweight, overweight and obesity compared with normal weight in relation to incident dementia were: 1.36 (1.07, 1.73), 0.88 (0.60, 1.27) and 1.42 (0.93, 2.18) respectively. Pooled ORs and 95% CI for obesity and incident Alzheimer's disease (AD) and vascular dementia were 1.80 (1.00, 3.29) vs. 1.73 (0.47, 6.31) and were stronger in studies with long follow-up (>10 years) and young baseline age (<60 years). Weight gain and high WC or skin-fold thickness increased risks of dementia in all included studies. The meta-analysis shows a moderate association between obesity and the risks for dementia and AD. Future studies are needed to understand optimal weight and biological mechanisms.

### Reference

Beydoun MA, et al. Obesity and central obesity as risk factors for incident dementia and its subtypes: a systematic review and meta-analysis. *Obesity Reviews*, 2008, 9:204-218.



## High cholesterol in midlife increases dementia risk

*Date published: May 2008*

### Main Message

This review of 18 studies found consistent associations between high midlife total cholesterol (TC) and increased risk of Alzheimer's disease (AD), and high midlife TC and increased risk of any dementia. There was no evidence supporting an association between late-life TC and AD, or between late-life TC and any dementia. No study reported a significant association between TC and vascular dementia (VaD). The results suggest the effect of TC on dementia risk occurs in midlife, and that there may be different cardiovascular risk factor profiles for AD and VaD.

### Abstract

The relationships between total serum cholesterol (TC) and dementia and between TC and cognitive decline were investigated in a systematic review of 18 prospective studies. Follow-ups ranged from 3 to 29 years, and included a total of 14,331 participants evaluated for Alzheimer disease (AD), 9,458 participants evaluated for Vascular dementia (VaD), 1,893 participants evaluated for cognitive decline, and 4,793 participants evaluated for cognitive impairment. Compatible results were pooled using meta-analysis. Consistent associations between high midlife TC and increased risk of AD, and high midlife TC and increased risk of any dementia were found. There was no evidence supporting an association between late-life TC and AD, or between late-life TC and any dementia. No study reported a significant association between TC (measured in midlife or late-life) and VaD. An association between high midlife TC and cognitive impairment was found but there was only weak evidence for an association between TC and cognitive decline. Two of seven studies reporting data on the interaction between TC and apolipoprotein e4-allele had significant effects. Results suggest the effect of TC on dementia risk occurs in midlife but not late-life, and that there may be different cardiovascular risk factor profiles for AD and VaD. Results from additional studies involving long-term follow-up of midlife samples will allow for clarification of the association between age, TC and risk of specific types of dementia. These data are required to inform recommendations of modulation of cholesterol to reduce or delay dementia risk.

### Reference

Anstey KJ, et al. Cholesterol as a risk factor for dementia and cognitive decline: a systematic review of prospective studies with meta-analysis. *American Journal of Geriatric Psychiatry*, 2008, 16:343-354.



## Vascular risk factors in midlife increase dementia risk

*Date published: May 2008*

### Main Message

This review found that type 2 diabetes, high blood pressure, obesity and high cholesterol are each associated with around a 50% increased risk of dementia. High blood pressure, obesity and high cholesterol measured at midlife were associated with the largest increase in risk. This review shows that vascular risk factors should be regarded as a major target for preventive measures, and that timing of such measures appears to be critical.

### Abstract

Vascular risk factors, such as type 2 diabetes, hypertension, obesity and dyslipidaemia often co-occur. Each of these factors has been associated with an increased risk of dementia, but it is uncertain which factor imposes the greatest risk. Moreover, the effect of age at time of exposure may differ across factors. This paper systematically reviews the evidence for the association of each of these risk factors with dementia. Longitudinal population-based studies that assessed the incidence of dementia in relation to diabetes (n=14), hypertension (n=13), dyslipidaemia (n=8) or obesity (n=9) were included. All four risk factors were indeed associated with an increased risk of dementia, but the results of studies on diabetes and obesity were most consistent. The magnitude of the effects was comparable across the risk factors, with odds ratios for 'any dementia' around 1.5. For hypertension, obesity and dyslipidaemia age appeared to modulate the association: the risk of dementia was generally largest in studies that measured the risk factor in midlife (compared to late life) and had a long follow-up time. At midlife, the population attributable risk of dementia was highest for hypertension, up to 30% of cases of late life dementia. Later in life diabetes appears to convey the highest risk of dementia. This review shows that vascular risk factors should be regarded as a major target for preventive measures, but that timing of such measures appears to be critical.

### Reference

Kloppenborg RP, et al. Diabetes and other vascular risk factors for dementia: which factor matters most? A systematic review. *European Journal of Pharmacology*, 2008, 585:97-108.



## SECTION TWO – STUDIES

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### Obesity in old age is not associated with greater dementia risk

**Date published:** December 2008

#### Main Message

In 605 people aged 65 and older, followed up for 8 years, those with higher BMI were less likely to develop dementia. On average, for each unit increase in BMI score, the risk of dementia was reduced by 8%. High BMI scores in late life should not necessarily be considered to be a risk factor for dementia.



#### Abstract

**OBJECTIVES:** To describe the association between body mass index (BMI) and dementia risk in older persons.

**DESIGN:** Prospective population-based study, with 8 years of follow-up.

**SETTING:** The municipality of Lieto, Finland, 1990/91 and 1998/99.

**PARTICIPANTS:** Six hundred five men and women without dementia aged 65 to 92 at baseline (mean age 70.8).

**MEASUREMENTS:** Weight and height were measured at baseline and at the 8-year follow-up. Dementia was clinically assessed according to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, criteria.

**RESULTS:** Eighty-six persons were diagnosed with dementia. Cox regression analyses, adjusted for age, sex, education, cardiovascular diseases, smoking, and alcohol use, indicated that, for each unit increase in BMI score, the risk of dementia decreased 8% (hazard ratio (HR)=0.92, 95% confidence interval (CI)=0.87-0.97). This association remained significant when individuals who developed dementia early during the first 4 years of follow-up were excluded from the analyses (HR=0.93, 95% CI=0.86-0.99). Women with high BMI scores had a lower dementia risk (HR=0.90, 95% CI=0.84-0.96). Men with high BMI scores also tended to have a lower dementia risk, although the association did not reach significance (HR=0.95, 95% CI=0.84-1.07).

**CONCLUSION:** Older persons with higher BMI scores have less dementia risk than their counterparts with lower BMI scores. High BMI scores in late life should not necessarily be considered to be a risk factor for dementia.

#### Reference

Dahl AK, et al. Overweight and obesity in old age are not associated with greater dementia risk. *Journal of the American Geriatrics Society*, 2008, 56:2261-2266.



## Cognitive reserve and Alzheimer's disease

**Date published:** November 2008

### Main Message

This study found that in people with high brain amyloid levels (measured with PiB PET scanning), those with more years of education (indicating higher cognitive reserve) performed better on a range of cognitive tests. The results support the hypothesis that cognitive reserve protects cognitive function in the presence of Alzheimer's disease pathological burden.

### Abstract

**OBJECTIVE:** To evaluate the cognitive reserve hypothesis by examining whether individuals of greater educational attainment have better cognitive function than individuals with less education in the presence of elevated fibrillar brain amyloid levels.

**DESIGN, SETTING, AND PARTICIPANTS:** Uptake of carbon 11-labeled Pittsburgh Compound B ( $[(11)\text{C}]\text{PiB}$ ) was measured for participants assessed between August 15, 2003, and January 8, 2008, at the Washington University Alzheimer's Disease Research Center and diagnosed either as nondemented ( $n = 161$ ) or with dementia of the Alzheimer type ( $n = 37$ ). Multiple regression was used to determine whether  $[(11)\text{C}]\text{PiB}$  uptake interacted with level of educational attainment to predict cognitive function.

**MAIN OUTCOME MEASURES:** Scores on the Clinical Dementia Rating sum of boxes, Mini-Mental State Examination, and Short Blessed Test and individual measures from a psychometric battery.

**RESULTS:** Uptake of  $[(11)\text{C}]\text{PiB}$  interacted with years of education in predicting scores on the Clinical Dementia Rating sum of boxes ( $P = .003$ ), the Mini-Mental State Examination ( $P < .001$ ), the Short Blessed Test ( $P = .03$ ), and a measure of verbal abstract reasoning and conceptualization ( $P = .02$ ) such that performance on these measures increased with increasing education for participants with elevated PiB uptake. Education was unrelated to global cognitive functioning scores among those with lower PiB uptake.

**CONCLUSION:** The results support the hypothesis that cognitive reserve influences the association between Alzheimer disease pathological burden and cognition.

### Reference

Roe CM, et al. Alzheimer disease and cognitive reserve: variation of education effect with carbon 11-labeled Pittsburgh Compound B uptake. *Archives of Neurology*, 2008, 65:1467-1471.





## Resistance training benefits cognition

*Date published: November 2008*

### Main Message

This review concluded that three recent randomized exercise trials involving resistance training among seniors provide evidence that resistance training may have cognitive benefits. The authors suggest clinicians should consider encouraging their clients to undertake both aerobic-based exercise training and resistance training not only for physical health but also because of the almost certain benefits for brain health.

### Abstract

In recent years, there has been a strong interest in physical activity as a primary behavioural prevention strategy against cognitive decline. A number of large prospective cohort studies have highlighted the protective role of regular physical activity in lowering the risk of cognitive impairment and dementia. The majority of prospective intervention studies of exercise and cognition to date have focused on aerobic-based exercise training. These studies highlight that aerobic-based exercise training enhances both brain structure and function. However, it has been suggested that other types of exercise training, such as resistance training, may also benefit cognition. The purpose of this brief review is to examine the evidence regarding resistance training and cognitive benefits. Three recent randomized exercise trials involving resistance training among seniors provide evidence that resistance training may have cognitive benefits. Resistance training may prevent cognitive decline among seniors via mechanisms involving IGF-1 and homocysteine. A side benefit of resistance training, albeit a very important one, is its established role in reducing morbidity among seniors. Resistance training specifically moderates the development of sarcopenia. The multifactorial deleterious sequelae of sarcopenia include increased falls and fracture risk as well as physical disability. Thus, clinicians should consider encouraging their clients to undertake both aerobic-based exercise training and resistance training not only for 'physical health' but also because of the almost certain benefits for 'brain health'.

### Reference

Liu-Ambrose T, et al. Exercise and cognition in older adults: Is there a role for resistance training programs? *British Journal of Sports Medicine*, 2008. Published Online 19 November 2008. doi:10.1136/bjism.2008.055616.



## Education reduces risk of Alzheimer's disease

**Date published:** November 2008

### Main Message

This study looked at education levels in people with Alzheimer's disease (AD) and matched healthy controls, and controlled for the presence of the APOE epsilon4 allele, which increases risk. Compared to those with 6-7 years of education, those with 8-9 years were significantly less likely to have AD, and chances were reduced even further for those with 10-18 years. Education had a consistently protective effect on the risk of developing clinical AD.

### Abstract

**OBJECTIVE:** To estimate the effect of education on the risk of Alzheimer's disease (AD).  
**METHODS:** 373 patients diagnosed with AD and 559 healthy control individuals without first degree relatives with known dementia, were included in a case-control study (2003-2006). All individuals were genotyped for APOE alleles. Odds ratio (OR) for developing AD was calculated by binary logistic regression, with the number of APOE epsilon 4 alleles and educational level as covariates. Analyses were carried out separately for men and women and for different age groups.

**RESULTS:** Carriers of one APOE epsilon 4 allele had OR of 4.2, and carriers of two APOE epsilon 4 alleles OR of 12.4 for developing AD. When adjusted for the number of APOE epsilon 4 alleles, OR for developing AD was significantly reduced in participants with 8-9 years of education compared to those with only 6-7 years, and was reduced further for those with 10-18 years of education. These findings were obtained for all the age groups studied and for both men and women.

**CONCLUSIONS:** Education had a consistently protective effect on the risk of developing clinical AD in a dose-dependent manner in both men and women, and in all age groups, also when adjusting for the number of APOE epsilon 4 alleles. Male gender was protective, probably at least in part because of a higher educational level.

### Reference

Sando SB, et al. Risk-reducing effect of education in Alzheimer's disease. *International Journal of Geriatric Psychiatry*, 2008, 23:1156-1162.



## Education and occupation contribute to brain reserve

*Date published: October 2008*



### Main Message

This study found that for people with Alzheimer's disease (AD), with similar severity of cognitive impairment, those with higher levels of education and who worked in more mentally demanding occupations had more brain damage. This suggests they experienced less cognitive decline as a result of the brain changes occurring. These findings add to others that suggest complex mental activity over the lifespan contributes to brain reserve, reducing the severity and delaying the clinical expression of AD pathology.

### Abstract

**BACKGROUND:** Previous reports have shown that higher education is associated with more severe brain pathology in patients with Alzheimer disease (AD), suggesting that these individuals have a functional reserve provided by education, which masks the clinical expression of a higher degree of neurodegeneration. It is unknown if a similar reserve mechanism exists in patients with amnesic mild cognitive impairment (aMCI). The aim of this study was to assess the impact of education and occupation on brain glucose metabolism (rCMRglc) measured with FDG-PET in aMCI and in a very large sample of subjects with probable AD (pAD).

**METHODS:** A total of 242 patients with pAD, 72 with aMCI, and 144 healthy controls participated in the study. At follow-up, 21 subjects with aMCI progressed to AD. A regression analysis was conducted (SPM2), with education and occupation as independent variables, and rCMRglc as dependent variable, adjusting for demographic data, global cognitive status, and neuropsychological scores.

**RESULTS:** The analysis showed a significant association between higher education/occupation and lower rCMRglc in posterior temporoparietal cortex and precuneus in pAD and aMCI converters, and no correlation in aMCI nonconverters and healthy controls. This means that, when submitted to FDG-PET for diagnostic evaluation, pAD and aMCI converters with higher education/occupation had, for comparable cognitive impairment, a more severe rCMRglc reduction than the ones with lower education/occupation.

**CONCLUSIONS:** This study suggests that education and occupation may be proxies for brain functional reserve, reducing the severity and delaying the clinical expression of Alzheimer disease (AD) pathology. The results in aMCI converters suggest that functional reserve is already at play in the prodementia phase of AD.

### Reference

Garibotto V, et al. Education and occupation as proxies for reserve in aMCI converters and AD: FDG-PET evidence. *Neurology*, 2008, 71:1342-1349.



## Midlife diabetes increases the risk of dementia

**Date published:** October 2008



### Main Message

In a group of 13,693 people over the age of 65, a history of diabetes was associated with an 89% increased risk of any dementia, 69% increased risk of Alzheimer's disease and 117% increased risk of vascular dementia. The increase in risk was especially strong for diabetes occurring in midlife.

### Note

This is yet another study highlighting the importance of controlling vascular risk factors from an early age.

### Abstract

**OBJECTIVE:** We aimed to verify the association between diabetes and the risk of dementia, Alzheimer disease (AD) and vascular dementia (VaD) in twins, and to explore whether genetic and early-life environmental factors could contribute to this association.

**RESEARCH DESIGN AND METHODS:** This study included 13,693 twin individuals aged  $\geq 65$ . Dementia was diagnosed according to DSM-IV criteria. Information on diabetes was collected from the inpatient registry, and self- or informant-reported history of diabetes. Data were analyzed following two strategies: 1) unmatched case-control analysis for all participants using generalized estimating equation (GEE) models, and 2) co-twin matched case-control analysis for dementia-discordant twin pairs using conditional logistic regression.

**RESULTS:** Of all participants, 467 were diagnosed with dementia including 292 AD and 105 VaD cases, and 170 were diagnosed with questionable dementia. Diabetes was present in 1,396 subjects. In GEE models, diabetes was associated with adjusted odds ratios (ORs) (95% CI) of 1.89 (1.51-2.38) for dementia, 1.69 (1.16-2.36) for AD and 2.17 (1.36-3.47) for VaD. Compared to late-life diabetes (onset age  $\geq 65$ ), the risk effect of midlife diabetes (onset age  $< 65$ ) on dementia was stronger. Conditional logistic analysis of 210 dementia-discordant twin pairs led to ORs of 2.41 (1.05-5.51) and 0.68 (0.30-1.53) for dementia related to mid- and late-life diabetes respectively.

**CONCLUSIONS:** Diabetes increases the risk of Alzheimer disease and vascular dementia. The risk is stronger when diabetes occurs at midlife than in late-life. Genetic and early-life environmental factors might contribute to the late-life diabetes-dementia association, but could not account for the midlife diabetes-dementia association.

### Reference

Xu W, et al. Mid- and late-life diabetes in relation to the risk of dementia: a population-based twin study. *Diabetes*, 2008, DOI: 10.2337/db08-0586



## Central obesity in midlife increases risk of dementia

**Date published:** September 2008

### Main Message

In a group of 6,563 people, larger sagittal abdominal diameter (a measure of abdominal or central obesity) measured at midlife was associated with an almost 3-fold increased risk of developing dementia decades later.

### Abstract

**BACKGROUND:** Numerous reports show that a centralized distribution of adiposity is a more dangerous risk factor for cardiovascular disease and diabetes than total body obesity. No studies have evaluated whether the same pattern exists with dementia. The objective was to evaluate the association between midlife central obesity and risk of dementia three decades later.

**METHODS:** A longitudinal analysis was conducted of 6,583 members of Kaiser Permanente of Northern California who had their sagittal abdominal diameter (SAD) measured in 1964 to 1973. Diagnoses of dementia were from medical records an average of 36 years later, January 1, 1994, to June 16, 2006. Cox proportional hazard models adjusted for age, sex, race, education, marital status, diabetes, hypertension, hyperlipidemia, stroke, heart disease, and medical utilization were conducted.

**RESULTS:** A total of 1,049 participants (15.9%) were diagnosed with dementia. Compared with those in the lowest quintile of SAD, those in the highest had nearly a threefold increased risk of dementia (hazard ratio, 2.72; 95% CI, 2.33-3.33), and this was only mildly attenuated after adding body mass index (BMI) to the model (hazard ratio, 1.92; 95% CI, 1.58-2.35). Those with high SAD (>25 cm) and normal BMI had an increased risk (hazard ratio, 1.89; 95% CI, 0.98-3.81) vs those with low SAD (<25 cm) and normal BMI (18.5-24.9 kg/m<sup>2</sup>), whereas those both obese (BMI >30 kg/m<sup>2</sup>) and with high SAD had the highest risk of dementia (HR, 3.60; 95% CI, 2.85-4.55).

**CONCLUSIONS:** Central obesity in midlife increases risk of dementia independent of diabetes and cardiovascular comorbidities. Fifty percent of adults have central obesity; therefore, mechanisms linking central obesity to dementia need to be unveiled.

### Reference

Whitmer RA, et al. Central obesity and increased risk of dementia more than three decades later. *Neurology*, 2008, 71:1057-1064.



## Impaired insulin response increases dementia risk

**Date published:** September 2008

### Main Message

In this study, 2,322 people underwent insulin response measures when they were 50 years old. Impaired insulin response at midlife was associated with an increased risk of Alzheimer's disease (AD) and any dementia up to 35 years later.

### Note

This study highlights the importance of checking for and controlling insulin resistance and diabetes from midlife.

### Abstract

**OBJECTIVE:** Subjects with diabetes are reported to have an increased risk of dementia and cognitive impairment. However, the underlying causes remain unknown. We investigated the longitudinal associations between midlife insulin secretion, glucose metabolism, and the subsequent development of Alzheimer disease (AD) and dementia.

**METHODS:** The population-based Uppsala Longitudinal Study of Adult Men started 1970 when the 2,322 participants were 50 years old. Investigation at baseline included determinations of acute insulin response and glucose tolerance using the IV glucose tolerance test and Homeostasis Model Assessment insulin resistance index. During a median follow up of 32 years, 102 participants were diagnosed with AD, 57 with vascular dementia, and 394 with any dementia or cognitive impairment. Associations were analyzed using Cox proportional hazard models.

**RESULTS:** A low insulin response at baseline was associated with a higher cumulative risk of AD (hazard ratio for 1 SD decrease, 1.31; 95% CI, 1.10-1.56) also after adjustment for age, systolic blood pressure, body mass index, serum cholesterol, smoking, education level, and insulin resistance. This association was stronger in subjects without the APOE epsilon4 allele. Impaired glucose tolerance increased the risk of vascular dementia (hazard ratio for 1 SD decrease, 1.45; 95% CI, 1.05-2.00) but not AD. Impaired insulin secretion, glucose intolerance, and estimates of insulin resistance were all associated with higher risk of any dementia and cognitive impairment.

**CONCLUSIONS:** In this longitudinal study, impaired acute insulin response at midlife was associated with an increased risk of Alzheimer disease (AD) up to 35 years later suggesting a causal link between insulin metabolism and the pathogenesis of AD.

### Reference

Ronnemaa E, et al. Impaired insulin secretion increases the risk of Alzheimer disease. *Neurology*, 2008, 71:1065-1071.



## Midlife cognitive activity reduces dementia risk

**Date published:** September 2008

### Main Message

In 294 male twins, participation in a range of cognitively and socially engaging activities in midlife reduced risk for dementia and Alzheimer's disease decades later. The protective effect of cognitive activity was strongest in those at greater genetic risk (APOE epsilon4 allele carriers).

### Note

Midlife physical activity did not modify dementia risk in this study, but has been shown to reduce risk in some other studies.

### Abstract

**BACKGROUND:** This was a prospective study of dementia to elucidate mechanisms of disease risk factors amenable to modification and specifically to determine whether midlife cognitive and physical leisure activities are associated with delayed onset or reduced risk of dementia within older male twin pairs.

**METHODS:** The co-twin control design used prospectively collected exposure information to predict risk of dementia 20 to 40 years later. The subjects were community-dwelling and nursing home residents living throughout the continental United States. We studied 147 male twin-pairs who were discordant for dementia or age of dementia onset and were members of the National Academy of Sciences-National Research Council Twin Registry of World War II veterans and participants in the Duke Twins Study of Memory in Aging. The main outcome measure was diagnosed dementia by using a two-stage screen and full clinical evaluation. Conditional odds ratios were estimated for the association between midlife leisure activities and late-life dementia.

**RESULTS:** Greater midlife cognitive activity was associated with a 26% risk reduction for dementia onset. Protective effects were most robust in monozygotic twin pairs, where genetic and early-life influences were most tightly controlled, and for activities that were often cognitive and social in nature. Cognitive activity was particularly protective among monozygotic twin pairs carrying the apolipoprotein E epsilon4 allele, with a 30% risk reduction. Midlife physical activity did not modify dementia risk.

**CONCLUSIONS:** Participation in a range of cognitively and socially engaging activities in midlife reduced risk for dementia and AD in twins discordant for onset, particularly among twin pairs at elevated genetic risk, and might be indicative of an enriched environment.

### Reference

Carlson MC, et al. Midlife activity predicts risk of dementia in older male twin pairs. *Alzheimer's & Dementia*, 2008, 4:324-331.



## Blood pressure treatment in the elderly may reduce dementia risk

**Date published:** August 2008



### Main Message

In this study of people 80 years and older with hypertension (high blood pressure), those treated with antihypertensive drugs for 2 years, were not significantly less likely to develop dementia. However, when data from this study were combined with data from similar studies, a significant protective effect was found for antihypertensive treatment. Elderly people with hypertension should be treated to reduce the risk of stroke and cardiovascular disease, and treatment may also reduce dementia risk.

### Note

This study was stopped after 2 years because of the beneficial effects of treatment on stroke and mortality. The study didn't definitively answer the questions about dementia risk, but it is unethical to not provide treatment given its benefits in other areas, so future clinical trials of this nature may not be feasible.

### Abstract

**BACKGROUND:** Observational epidemiological studies have shown a positive association between hypertension and risk of incident dementia; however, the effects of antihypertensive therapy on cognitive function in controlled trials have been conflicting, and meta-analyses of the trials have not provided clear evidence of whether antihypertensive treatment reduces dementia incidence. The Hypertension in the Very Elderly trial (HYVET) was designed to assess the risks and benefits of treatment of hypertension in elderly patients and included an assessment of cognitive function.

**METHODS:** Patients with hypertension (systolic pressure 160-200 mm Hg; diastolic pressure <110 mm Hg) who were aged 80 years or older were enrolled in this double-blind, placebo-controlled trial. Participants were randomly assigned to receive 1.5 mg slow release indapamide, with the option of 2-4 mg perindopril, or placebo. The target systolic blood pressure was 150 mm Hg; the target diastolic blood pressure was 80 mm Hg. Participants had no clinical diagnosis of dementia at baseline, and cognitive function was assessed at baseline and annually with the mini-mental state examination (MMSE). Possible cases of incident dementia (a fall in the MMSE score to <24 points or a drop of three points in 1 year) were assessed by standard diagnostic criteria and expert review. The trial was stopped in 2007 at the second interim analysis after treatment resulted in a reduction in stroke and total mortality. Analysis was by intention to treat. The trial is registered with ClinicalTrials.gov, number NCT00122811.

**FINDINGS:** 3336 HYVET participants had at least one follow-up assessment (mean 2.2 years) and were included: 1687 participants were randomly assigned to the treatment group and 1649 to the placebo group. Only five reports of adverse effects were attributed to the medication: three in the placebo group and two in the treatment group. The mean decrease in systolic blood pressure between the treatment and placebo groups at 2 years was systolic -15 mm Hg,  $p < 0.0001$ ; and diastolic -5.9 mm Hg,  $p < 0.0001$ . There were 263 incident cases of dementia. The rates of incident dementia were 38 per 1000 patient-years in the placebo group and 33 per 1000 patient-years in the treatment group. There was no significant difference between treatment and placebo groups (hazard ratio [HR] 0.86, 95% CI 0.67-1.09); however, when these data were combined in a meta-analysis with other placebo-controlled trials of antihypertensive treatment, the combined risk ratio favoured treatment (HR 0.87, 0.76-1.00,  $p = 0.045$ ).

**INTERPRETATION:** Antihypertensive treatment in elderly patients does not statistically reduce incidence of dementia. This negative finding might have been due to the short follow-up, owing to the early termination of the trial, or the modest effect of treatment. Nevertheless, the HYVET

findings, when included in a meta-analysis, might support antihypertensive treatment to reduce incident dementia.

**Reference**

Peters R, et al. Incident dementia and blood pressure lowering in the Hypertension in the Very Elderly Trial cognitive function assessment (HYVET-COG): a double-blind, placebo controlled trial. *Lancet Neurology*, 2008, 7:683-689.



## Social network size and dementia risk

*Date published: July 2008*

### Main Message

In 2249 women aged 78 or older, women with larger social networks had a 36% reduced risk of dementia. Other studies have also shown protective effects of larger social network size.

### Abstract

**OBJECTIVES:** We examined whether social networks had a protective association with incidence of dementia among elderly women.

**METHODS:** We prospectively studied 2249 members of a health maintenance organization who were 78 years or older, were classified as free of dementia in 2001, and had completed at least 1 follow-up interview in 2002 through 2005. We used the Telephone Interview for Cognitive Status-modified, the Telephone Dementia Questionnaire, and medical record review to assess cognitive status. We used the Lubben Social Network Scale-6 to assess social network. We estimated hazard ratios for incident dementia with Cox proportional hazards models, adjusting for age at entry, education, hormone use, cognitive status scores, and health conditions.

**RESULTS:** We identified 268 incident cases of dementia during follow-up. Compared with women with smaller social networks, the adjusted hazard ratio for incident dementia in women with larger social networks was 0.74 (95% confidence interval=0.57, 0.97).

**CONCLUSIONS:** Our findings suggest that larger social networks have a protective influence on cognitive function among elderly women. Future studies should explore which aspects of social networks are associated with dementia risk and maintenance of cognitive health.

### Reference

Crooks VC, et al. Social network, cognitive function, and dementia incidence among elderly women. *American Journal of Public Health*, 2008, 98:1221-1227.



## Social integration associated with preserved memory function

*Date published: July 2008*

### Main Message

In 16,638 older Americans followed up for 6 years, higher levels of social integration were associated with slower memory decline. The effect of social integration on memory loss was largest in those with lower levels of education.

### Abstract

**OBJECTIVES:** We tested whether social integration protects against memory loss and other cognitive disorders in late life in a nationally representative US sample of elderly adults, whether effects were stronger among disadvantaged individuals, and whether earlier cognitive losses explained the association (reverse causation).

**METHODS:** Using data from the Health and Retirement Study (N = 16,638), we examined whether social integration predicted memory change over 6 years. Memory was measured by immediate and delayed recall of a 10-word list. Social integration was assessed by marital status, volunteer activity, and frequency of contact with children, parents, and neighbors. We examined growth-curve models for the whole sample and within subgroups.

**RESULTS:** The mean memory score declined from 11.0 in 1998 to 10.0 in 2004. Higher baseline social integration predicted slower memory decline in fully adjusted models ( $P < .01$ ). Memory among the least integrated declined at twice the rate as among the most integrated. This association was largest for respondents with fewer than 12 years of education. There was no evidence of reverse causation.

**CONCLUSIONS:** Our study provides evidence that social integration delays memory loss among elderly Americans. Future research should focus on identifying the specific aspects of social integration most important for preserving memory.

### Reference

Ertel KA, et al. Effects of social integration on preserving memory function in a nationally representative US elderly population. *American Journal of Public Health*, 2008, 98:1215-1220.



## Physical activity in older age reduces vascular dementia risk

**Date published:** May 2008

### Main Message

In 749 people aged 65 and older, higher amounts of walking, moderate physical activities and total physical activity were associated with 73, 71 and 76% reduced risk of vascular dementia, respectively.

### Note

In this study, physical activity was not associated with reduced risk of Alzheimer's disease. However, such an association has been shown in other studies.

### Abstract

**OBJECTIVE:** To examine the effect of physical activity on risk of developing Alzheimer disease (AD) and vascular dementia (VaD) in the elderly.

**METHODS:** Data are from a prospective population-based cohort of 749 Italian subjects aged 65 and older who, in 1999/2000, were cognitively normal at an extensive assessment for clinically overt and preclinical dementia and, in 2003/2004, underwent follow-up for incident dementia. Baseline physical activity was measured as energy expenditure on activities of different intensity (walking, stair climbing, moderate activities, vigorous activities, and total physical activity).

**RESULTS:** Over 3.9 +/- 0.7 years of follow-up there were 86 incident dementia cases (54 AD, 27 VaD). After adjustment for sociodemographic and genetic confounders, VaD risk was significantly lower for the upper tertiles of walking (hazard ratio [HR] 0.27, 95% CI 0.12 to 0.63), moderate (HR 0.29, 95% CI 0.12 to 0.66), and total physical activity (HR 0.24, 95% 0.11 to 0.56) compared to the corresponding lowest tertile. The association persisted after accounting for vascular risk factors and overall health status. After adjustment for sociodemographic and genetic confounders, AD risk was not associated with measures of physical activity and results did not change after further adjustment for vascular risk factors and overall health and functional status.

**CONCLUSIONS:** In this cohort, physical activity is associated with a lower risk of vascular dementia but not of Alzheimer disease. Further research is needed about the biologic mechanisms operating between physical activity and cognition.

### Reference

Ravaglia G, et al. Physical activity and dementia risk in the elderly: findings from a prospective Italian study. *Neurology*, 2008, 70:1786-1794.



## Physical activity associated with reduced dementia risk in older men

**Date published:** May 2008

### Main Message

In 2263 men aged over 70 and followed up for an average of 6 years, increased physical activity was associated with reduced risk of dementia. This was especially so for men with poor physical function, for whom high and moderate levels of physical activity were associated with reduced risk of dementia and Alzheimer's disease.

### Note

The effects were not significant in men with moderate or high physical function, but this doesn't mean they wouldn't benefit from physical activity.

### Abstract

**BACKGROUND:** Although evidence is accumulating for a protective effect of late life physical activity on the risk of dementia, the findings are inconsistent, especially in men. We examined the association of late life physical activity and the modifying effect of physical function with future risk of dementia in a well-characterized cohort of elderly men participating in the Honolulu-Asia Aging Study (HAAS).

**METHODS:** Physical activity by self-report and performance-based physical function was assessed in 2263 men aged 71-92 years without dementia at the baseline examination of the HAAS in 1991-1993. Follow-up for incident dementia occurred at repeat examinations conducted in 1994-1996 and 1997-1999. Analyses were based on Cox proportional hazards models with adjustment for potential confounders, including age, baseline cognitive function, education, and apolipoprotein E genotype.

**RESULTS:** There were 173 incident cases of dementia with a mean follow-up of 6.1 years. Although the incidence of dementia tended to decline with increasing physical activity and function, there was a significant interaction between the latter two factors on dementia risk ( $p = .022$ ). For men with low physical function, high levels of physical activity were associated with half the risk of dementia versus men who were the least active (hazard ratio [HR], 0.50; 95% confidence interval [CI], 0.28-0.89), with a moderate level of physical activity also providing a protective effect (HR, 0.57; 95% CI, 0.32-0.99). Risk of dementia and Alzheimer's disease declined significantly with increasing physical activity. Findings persisted after age and risk factor adjustment. Similar associations were absent in men with moderate and high physical function.

**CONCLUSIONS:** In elderly men with poor physical function, increasing general physical activity may potentially confer a protective effect or delay the onset for dementia.

### Reference

Taaffe DR, et al. Physical activity, physical function, and incident dementia in elderly men: the Honolulu-Asia Aging Study. *The Journals of Gerontology, Series A, Biological Sciences and Medical Sciences*, 2008, 63:529-535.



## Complex work reduces dementia risk

*Date published: April 2008*

### Main Message

In 3,557 older adults, a history of high complexity of work with people or things was associated with a reduced risk of any dementia and a reduced risk of vascular dementia.

### Note

In this study, there was no association between complexity of work and risk of Alzheimer's disease, but such an association has been demonstrated in other studies.

### Abstract

The authors evaluated the association of complexity of work with data, people, and things with the incidence of dementia, Alzheimer's disease, and vascular dementia in the Canadian Study of Health and Aging, while adjusting for work-related physical activity. The Canadian Study of Health and Aging is a 10-year population study, from 1991 to 2001, of a representative sample of persons aged 65 years or older. Lifetime job history allowed application of complexity scores and classification of work-related physical activity. Analyses included 3,557 subjects, of whom 400 were incident dementia cases, including 299 with Alzheimer's disease and 93 with vascular dementia. In fully adjusted Cox regression models, high complexity of work with people or things reduced risk of dementia (hazard ratios were 0.66 (95% confidence interval: 0.44, 0.98) and 0.72 (95% confidence interval: 0.52, 0.99), respectively) but not Alzheimer's disease. For vascular dementia, hazard ratios were 0.36 (95% confidence interval: 0.15, 0.90) for high complexity of work with people and 0.50 (95% confidence interval: 0.25, 1.00) for high complexity of work with things. Subgroup analyses according to median duration (23 years) of principal occupation showed that associations with complexity varied according to duration of employment. High complexity of work appears to be associated with risk of dementia, but effects may vary according to subtype.

### Reference

Kroger E, et al. Is complexity of work associated with risk of dementia? The Canadian Study of Health and Aging. *American Journal of Epidemiology*, 2008, 167:820-830.



## Midlife physical exercise reduces dementia risk

**Date published:** January 2008

### Main Message

For levels of exercise measured at midlife, light exercise was associated with a 37% reduced risk of dementia decades later and regular exercise with a 66% reduced risk. Exercise at midlife may reduce the odds of dementia in older adulthood, suggesting that exercise interventions should be explored as a potential strategy for delaying disease onset.

### Abstract

**BACKGROUND:** With the number of people with dementia increasing, identifying potential protective factors has become more important. We explored the association between physical exercise at midlife and subsequent risk of dementia among members of the HARMONY study. **METHODS:** Measures of exercise were obtained by the Swedish Twin Registry an average of 31 years prior to dementia assessment. Dementia was diagnosed using a two-stage procedure--screening for cognitive impairment followed by full clinical evaluation. We used two study designs: case-control analyses included 264 cases with dementia (176 had Alzheimer's disease) and 2870 controls; co-twin control analyses included 90 twin pairs discordant for dementia.

**RESULTS:** In case-control analyses, controlling for age, sex, education, diet (eating fruits and vegetables), smoking, drinking alcohol, body mass index, and angina, light exercise such as gardening or walking and regular exercise involving sports were associated with reduced odds of dementia compared to hardly any exercise (odds ratio [OR] = 0.63, 95% confidence interval [CI], 0.43-0.91 for light exercise; OR = 0.34, 95% CI, 0.16-0.72 for regular exercise). Findings were similar for Alzheimer's disease alone. In co-twin control analyses, controlling for education, the association between higher levels of exercise and lower odds of dementia approached significance (OR = 0.50, 95% CI, 0.23-1.06;  $p = .072$ ).

**CONCLUSIONS:** Exercise at midlife may reduce the odds of dementia in older adulthood, suggesting that exercise interventions should be explored as a potential strategy for delaying disease onset.

### Reference

Andel R, et al. Physical exercise at midlife and risk of dementia three decades later: a population-based study of Swedish twins. *The Journals of Gerontology, Series A, Biological Sciences and Medical Sciences*, 2008, 63:62-66.