

A Case-control Study to Identify the Risk Factors of Dementia among Clinically Diagnosed Patients in Kerala

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Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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ABSTRACT

Context: Dementia is one of the most significant challenges of the 21st century because of its health, social and economic impact. In India over 4.1 million people are affected. Dementia still remains a largely hidden problem in India. There is gross ignorance, neglect and scarce services for people with dementia and their families, especially in the disadvantaged parts of India.

Objective: To identify the risk factors of dementia among the residents of ARDSI (Alzheimer's and related Disorders Society of India) Centers in Kerala.

Materials and Methods: A case control study involving 51 clinically diagnosed dementia patients from four ARDSI Centers in Kerala were considered as cases and 102 age and gender matched controls were selected from neighborhood.

Using a pretested structured interview schedule the risk factors of dementia were identified.

Results: 51 cases and 102 controls participated in this study. The dementia patients who were in the 70–79 age group constituted 43%. Among the women with dementia 18% were widows. Multiple logistic regression analysis showed that important determinants of dementia were increasing age, married status, family history of dementia and hypertension.

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Conclusion: The public awareness about dementia in India is low. A better understanding & identification of the risk factors of dementia which would protect/reduce the risk of dementia is essential for controlling this silent epidemic.

Keywords: Dementia; case-control; Alzheimer's disease; risk factors; ARDSI.

1. INTRODUCTION

According to World health organization the developing countries of the world by 2025 will account for the majority of elders in the world, China and India contributing nearly a fifth [1]. India has 4.1 million people with Alzheimer's disease (AD) and related dementias and this is expected to double by the year 2030 [2]. Reports indicate that in 2010, more than half (57.7%) of all people with dementia lived in low and middle-income countries. This proportion is expected to rise to 63.4% in 2030 and to over 70% in 2050. The joint report by the World Health Organization and Alzheimer's Disease International which published these figures has gained wide international attention [3]. Dementia is a growing problem in aging population. Within the next five years, it is expected that the number of adults aged 65 and over will outnumber children under the age of 5 and by the year 2050 older adults will outnumber children under the age of 14 [4].

In India the number of people with Alzheimer's disease and other dementias is increasing every year because of the steady growth in the older population and stable increment in life expectancy and it is expected to increase two-fold by 2030 and three-fold by 2050 [5]. Dementia is characterized by loss of or decline in memory and other cognitive abilities and reduces the lifespan of affected people. Dementia is often associated with physical, mental and financial burden and evidence suggests that elderly people with dementia in developing countries do not often utilize health care services, and when they do, the health care system is often ill prepared to provide quality services for dementia. Around 10-37% of the elderly population with dementia in developing countries is classified as having potentially vulnerable living circumstances with requiring long-term and specialized care [6-12]. Approximately 2% of cases start before the age of 65 years [13]. After this, the prevalence doubles with every five year increment in age. Dementia is one of the major causes of disability in late-life.

Various risk factors have been found to be associated with dementia and Alzheimer's

disease. Of note, many recognized vascular risk factors for ischemic heart disease and/or stroke are also risk factors for dementia. Although some potentially reversible conditions such as hypothyroidism or vitamin B-12 deficiency are often considered to be causes of dementia, no more than 1.5% of cases of mild to moderate dementia are fully reversible [14]. Diabetes, hypertension, smoking and obesity have all been found to increase dementia risk. While vascular risk factors and cerebrovascular diseases clearly underlie vascular dementia, an etiological role for vascular changes in A β deposition and hence Alzheimer's disease remains unclear [15]. Alzheimer's disease is a complex disorder for which there is currently no known prevention or cure. Some research has generated hope that one day it might be possible to slow the progression of Alzheimer's disease, delay its symptoms or even prevent it from occurring at all. Although there is preliminary data to support the benefit of some interventions, such as physical activity and cardiovascular risk reduction, nothing at this time has definitively been shown to prevent Alzheimer's disease or other dementias.

Identification of risk factors for Alzheimer's disease is important because they can indicate lifestyle choices that can help reduce a person's chance of developing the disease. Some factors are beyond individual control, while other important risk factors can be reduced through appropriate lifestyle.

Despite the magnitude of this problem, there is gross negligence, neglect and scarce facilities for the care of people with dementia. Given the demographic transition and the disintegration of the joint families in many parts of the country, diseases such as dementia are emerging as a major public health challenge.

1.1 Objectives

To identify the risk factors of dementia among the residents of Alzheimer's and related Disorders Society of India (ARDSI) Centres in Kerala.

2. MATERIALS AND METHODS

The study was conducted among the residents of four ARDSI centres in Kerala after obtaining consent from the concerned authorities. ARDSI, established in 1992, is a non-government organization which has spearheaded the dementia movement in India. ARDSI has been in the forefront as a registered national, non-profit, voluntary organization engaged in the care, support, training and research of dementia since its inception in 1992. ARDSI is actively involved in developing services. Currently there is a Day Centre (Cochin) and three full time care homes (Cochin, Kunnamkulam, Calicut) for people with dementia run by the national office in Kerala, and another center is being run by the Thiruvananthapuram Chapter. Professional care is provided to the residents by trained carers round the clock. The staff provides various therapies to the residents such as cognitive stimulation, light exercises, yoga, music therapy and reality orientation. They were selected from four districts of Kerala namely Thiruvananthapuram, Kottayam, Ernakulam and Kozhikode. All the residents in these four centres were selected which accounted for fifty one clinically diagnosed dementia patients. The controls were people matched for age, socioeconomic status, education and they were 102 in number and were matched for age, gender, and socioeconomic status.

2.1 Study Design

The residents of the ARDSI centres had undergone a two phase study which included a screening phase and a diagnostic confirmation phase. The screening phase included an evaluation of the cognitive status using the MMSE (Mini Mental State Examination) the most commonly used and studied test which had acceptable accuracy [16] and the Pfeiffer questionnaire (SPMSQ) [17]. Individuals with a score of less than 24 points were considered positive and went to the following phase. Those people suspected of having dementia were evaluated by a Neurologist by using a structured history and clinical examination which included the CDR (Clinical Dementia Rating) scale. The Neuropsychiatric Inventory was used to evaluate the behavioural symptoms [18]. Further evaluation tests for reaching a diagnosis like blood investigations (Haemogram, Thyroid function Tests, Vitamin B12) and or a CT / MRI

was done. The final diagnosis of dementia was made based on the DSM-1V criteria (American Psychiatric Association).

The care co-ordinator of each centre was interviewed using structured interview response schedule. The details of each patient was well-documented on admission at the ARDSI centre and any further doubts were cleared by the immediate close respondents of the residents. The data base of the residents were obtained from the centres which included the socio-demographic data, the risk factors of dementia such as family history of dementia, diabetes, hypertension, smoking, alcoholism and head injury.

The controls were selected from neighbourhoods of the respective residents who were matched for age, gender, education. 102 controls were selected for the study.

The study was conducted for one month period from October –November 2011.

2.2 Statistical Analysis

The SPSS version16 for windows was used for the statistical analysis. The rates and ratios were calculated. Frequencies were calculated for each of the risk factors in cases of dementia and in controls. To evaluate the association between risk factors of dementia, multiple logistic regression was used and adjusted odds ratios were calculated. Univariate analysis of factors associated with cases and controls was created. In this model each of the risk factors like family history of dementia, diabetes, hypertension head injury and smoking were included. A second model was created and the risk factors like age, gender, marital status, smoking, and hypertension were included simultaneously to determine the independent effect of each one of them.

3. RESULTS

The study included 51 diagnosed cases of dementia and 102 controls who had no dementia. The socio-demographic factors of the participants are shown in Table 1. Among the cases 43% belonged to the 70-79 age group, 37.3% were graduates, 53% were married and 49% came from the high-income group. The proportion of unmarried people and widows/widowers were higher (47%) in the

dementia group when compared to the controls (17%).

Alzheimer's disease (AD) was the most commonest type of dementia among the cases- 74.5% (Fig. 1).

Among the socio-demographic factors age, marital status and family income showed a significant relationship to dementia. Increasing age was directly proportional to increase in the prevalence of dementia, Gender was not significantly associated with dementia. Poor education, unemployment and type of family had no significance to dementia in this study.

The effect of risk factors among cases and controls when examined showed that family history of dementia (<0.01) and hypertension (p=0.003) had an association with dementia (Table 2).

In the univariate model family history of dementia (OR = 3.17 p<0.003), hypertension (OR=3.29: p< 0.33), and head injury (OR= 3.04 p<0.033) were found to be risk factors of dementia (Table 3).

The multiple logistic regression analysis showed that the following risk factors had significant association with dementia (Table 4).

Table 1. Socio-demographic characteristics of cases and controls

Variable	Cases	Controls	P value
Age group			
50-59	3 (5.9%)	0 (0.0%)	
60-69	9 (17.6%)	62 (60.8%)	
70-79	22 (43.1%)	34 (33.3%)	< 0.001
80-89	16 (31.4%)	6 (5.9%)	
90-99	1 (2.0%)	0 (0.0%)	
Total	51 (100.0%)	102 (100.0%)	
Gender			
Male	26 (51.0%)	61 (59.8%)	
Female	25 (49.0%)	41 (40.2%)	0.306
Total	51 (100.0%)	102 (100.0%)	
Education			
Primary	9 (17.6%)	15 (14.7%)	
Secondary	16 (31.4%)	22 (21.6%)	
Graduate	19 (37.3%)	36 (35.3%)	0.178
Post graduate	7 (13.7%)	29 (28.4%)	
Total	51 (100.0%)	102 (100.0%)	
Occupation			
Unemployed	19 (37.3%)	32 (31.4%)	
Unskilled	1 (2.05)	10 (9.8%)	
Skilled	15 (29.4%)	22 (21.6%)	0.216
Professional	16 (31.4%)	38 (37.3%)	
Total	51 (100.0%)	102 (100.0%)	
Family income			
Low Income Group	2 (3.9%)	18 (17.6%)	
Middle Income Group	24 (47.1%)	37 (36.3%)	< 0.001
High Income Group	25 (49.0%)	47 (46.1%)	
Total	51 (100.0%)	102 (100.0%)	
Marital status			
Married	27 (52.9%)	83 (81.4%)	
Unmarried	4 (7.8%)	5 (4.9%)	< 0.001
Widow/Widower/Divorce	20 (39.2%)	14 (13.7%)	
Total	51 (100.0%)	102 (100.0%)	
Type of family			
Nuclear	29 (56.9%)	54 (52.9%)	
Joint	22 (43.1%)	48 (47.1%)	0.731

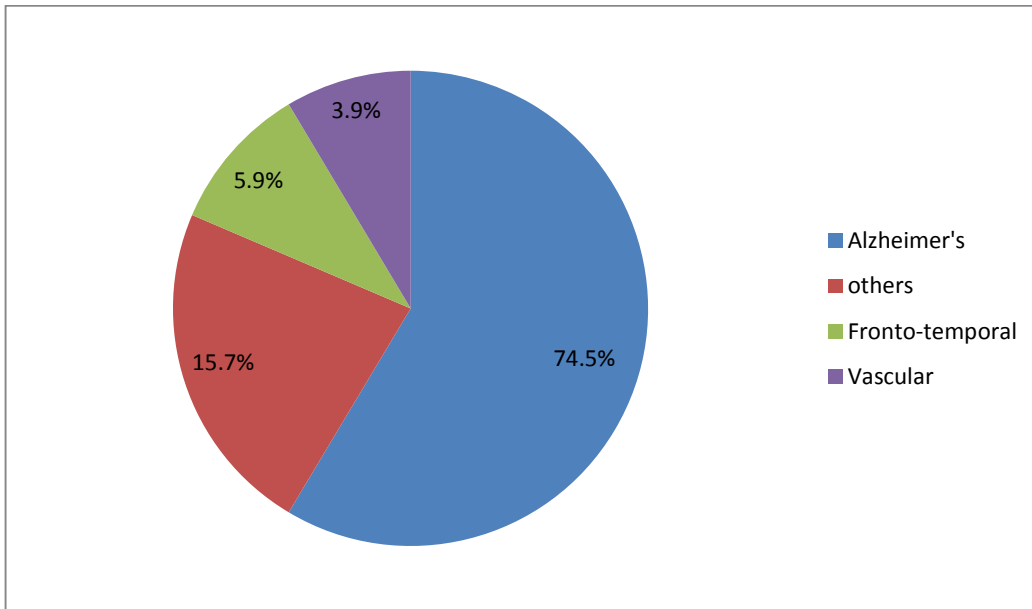


Fig. 1. Type of dementia cases

Table 2. Frequency of the risk factors in the study population

Habits	Cases	Controls	P value
Smoking	6 (11.8%)	12 (11.8%)	0.872
Alcoholism	2 (3.9%)	7 (6.9%)	
Both	4 (7.8%)	6 (5.9%)	
Nil	39 (76.5%)	77 (75.5%)	
Diabetes			0.603
Yes	19 (37%)	43 (42.2%)	
No	32 (63%)	59 (57.8%)	
Hypertension			0.003
Yes	13 (25%)	52 (51%)	
No	38 (75%)	50 (49%)	
Head Injury			0.333
Yes	2 (3.9%)	0	
No	49 (96.1%)	102 (100%)	
Family History			0.01
Yes	4 (7.8%)	0	
No	47 (92.2%)	102 (100%)	

Table 3. Univariate analysis of risk factor association with cases and controls

Characteristics	Categories	Cases	Controls	p value	Odds ratio (95% CI)
Family history of Dementia	Yes	4 (7.8%)	0 (0.0%)	0.01	3.170
	No	47 (92.2%)	102(100.0%)		
Diabetes	Yes	19 (37.3%)	43 (42.2%)	0.603	0.815
	No	32 (62.7%)	59 (57.8%)		
Hypertension	Yes	13 (25.5%)	52 (51.0%)	0.003	3.29
	No	38 (74.5%)	50 (49.0%)		
Head injury	Yes	1 (2.0%)	0 (0.0%)	0.033	3.040
	No	50 (98.0%)	102 (100%)		
Smoking	Smokers	10 (19.6%)	18 (17.6%)	0.826	1.12
	Non smokers	41 (80.4%)	84 (82.4%)		

Table 4. Regression model showing association with Alzheimer's disease

Characteristics	Ad. odds ratio (95% CI)	P value
Age	1.09 (0.161 – 4.195)	0.001
Marital status	6.103 (2.30 – 16.18)	0.001
Hypertension	0.279 (0.125 – 0.626)	0.002
Smoking	1.578 (0.561 – 4.395)	0.383
Gender	1.450 (0.582 – 3.611)	0.425

1. Increasing age
2. Being unmarried or widowed/widower
3. Hypertension

Family history of dementia showed a statistical significance in the univariate analysis but lost its significance in the multivariate analysis.

4. DISCUSSION

The objective of this study was to identify the risk factors of dementia among clinically diagnosed cases of dementia assessing socio-demographic, genetic, medical and lifestyle exposure. Since the dementia cases were already confirmed cases the problem of misdiagnosis could be avoided. The controls were selected within similar geographical region. Comparison was sought for age and socioeconomic factors between the cases and controls. The risk factors which were to be assessed were not matched.

The study showed that as age increases the risk of dementia also increase. Between 65 and 85 years of age, the prevalence doubles every 5.2 years following an exponential model. [19,20,21,22]. A meta-analysis that included 17 Chinese studies has also shown that the prevalence of dementia increases with age [23]. Our study supports this hypothesis as increasing age was a risk factor for dementia. Female gender was not an independent risk factor in our study as demonstrated by some authors [24]. However, others have not found differences between genders, and when it occurs is at very advanced ages (over 90 years of age [25]. Alzheimer's disease was the most common subtype of dementia among the study population which is at par with other studies [26]. In this study education did not show any relationship to the development of dementia whereas in some studies [27,28] lower education was a risk factor for the onset of dementia. Prevalence of dementia was seen more among the unmarried group when compared to the controls which was comparable to a community survey done in Kerala [29] where the prevalence was more among unmarried or single group which needs to be further explored. There was little difference

between cases and controls for educational attainment in a study done as part of the Rochester epidemiological study by Mary Beard et al. (2006). A family history of dementia is usually a risk factor for dementia. In this study it was significantly associated with dementia in the univariate model but lost its significance during the regression analysis which was consistent with some other studies [30–33]. Hypertension was an independent risk factor for dementia in this study. Other authors also have demonstrated a similar significant association [34]. Diabetes had no association with dementia in our study which was similar to the Canadian study of health and aging [35]. Traumatic brain injury can induce the early development of AD [36]. A meta-analysis that included 15 case-control studies has found that head injury is associated with an elevated risk of AD among men but not women [37]. We found no association of head injury with dementia in our study. A recent meta-analysis has shown that current smoking is associated significantly with an increased risk of AD but not with vascular dementia and cognitive decline [38] which was not found in this study. Two follow-up studies [39] in the United States and one in China [40] have reported a significant association between current smokers and the risk of dementia.

5. CONCLUSION AND RECOMMENDATIONS

The strength of our study was that it paved a way for better understanding of the risk factors and also identification of factors which protect or reduce the risk of dementia. Public awareness about dementia is low. Hence it has to be promoted. The key role of families of dementia patients & the caregivers should be recognized. Government policy for making dementia a health priority should be given importance.

6. LIMITATIONS

- The evaluated population size was small and the the strata of population selected

was mainly from the middle income group which might not represent the actual population.

- Kerala has a high prevalence of diabetes and hypertension.
- Since diabetes and hypertension are suspected risk factors of dementia matching was not done as its role in the study would have been eliminated.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Author has declared that no competing interests exist.

REFERENCES

1. World Health Organisation. W. Fact Sheet No.135. Geneva: World Health Organisation; Population ageing- A public health challenge; 1998.
2. World Alzheimer's Report; 2016.
3. WHO and Alzheimer's disease International: A public health priority. World Health Organization; 2012.
4. Population aging and health in India- Prediction based on census; 2011.
5. Tripathi MV, Vibha D. Risk factors of dementia in North India: A case-control study. *Aging and Mental Health*. 2012; 16(2):228-35
6. Ernst RL, Hay JW. The US economic and social costs of Alzheimer's disease revisited. *Am J Public Health* 1994;84: 1261-1264.
7. Dunkin J, Anderson-Hanley C. Dementia caregiver burden: A review of the literature and guidelines for assessment and intervention. *Neurology*. 1998;51(Suppl 1): S53-S60.
8. Brodaty H, Clarke J, Ganguli M, et al. Screening for cognitive impairment in general practice: Toward a consensus. *Alzheimer Dis Assoc Disord*.1998;12:1-13.
9. Grafstrom M, Fratiglioni L, Sandman P, Winblad B. Health and social consequences for relatives of demented and non-demented elderly. A population based study. *J Clin Epidemiol*. 1992;45: 861-870.
10. Schulz R, O'Brien A, Bookwala J, Fleissner K. Psychiatric and physical morbidity effects of dementia care giving: Prevalence, correlates, and causes. *Gerontologist*. 1995;35:771-791.
11. Hoyert DL, Kochanek KD, Murphy SL. Deaths: Final data for 1997. *National Vital Stat Rep*. 1999;47:1-104.
12. Gold DP, Reis MF, Markiewicz D, Andres D. When home caregiving ends: A longitudinal study of outcomes for caregivers of relatives with dementia. *J Am Geriatr Soc*. 1995;43:10-16.
13. Sternberg SA, Wolfson C, Baumgarten M. Undetected dementia in community-dwelling older people: The Canadian Study of Health and Aging. 2000;48(11).
14. Kipen E, Helme RD, Wark JD, et al. Bone density, Vitamin D nutrition, and parathyroid hormone levels in women with dementia. *J Am Geriatr Soc* 1995;43: 1088-91.
15. Starkstein SE, Almeida OP. Understanding cognitive impairment and dementia: Stroke study. *Curr Opin Psychiatry*. 2003;16:615-20.
16. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12: 189-198.
DOI: 10.1016/0022-3956(75)90026-6
17. Pfeiffer E. A short portable mental status questionnaire for the assessment of organic brain deficit in elderly patients. *J Am Geriatr Soc*. 1975;23:433-441.
18. Mega MS, Cummings JL, Fiorello T, Gornbein J. The spectrum of behavioral changes in Alzheimer's disease. *Neurology*. 1996;46:130-135.
19. von Strauss E, Viitanen M, De Ronchi D, Winblad B, Fratiglioni L. Aging and the occurrence of dementia: Findings from a population-based cohort with a large sample of nonagenarians. *Archives of Neurology*. 1999;56:587-592.

20. Borjesson-Hanson A, Edin E, Gislason T, Skoog I. The prevalence of dementia in 95 year olds. *Neurology*. 2004;63:2436–2438.
21. Ptok U, Papassotiropoulos A, Maier W, et al. Advanced parental age: A risk factor for Alzheimer's disease or depression in the elderly? *Int Psychogeriatric Journal*. 2000; 12:445–51.
22. Manubens JM, Martinez-Lage J. Prevalence of Alzheimer's disease and other dementing disorders in Pamplona, Spain. *Neuroepidemiology*. 1995;14:155–164.
DOI: 1159/000109791
23. Liu L, Guo XE, Zhou YQ, et al. Prevalence of dementia in China. *Dementia & Geriatric Cogn Disord*. 2003;15:226–30.
24. Prencipe M, et al. Prevalence of dementia in an elderly rural population: Effects of age, sex, and education. *J Neurol Neurosurg Psychiatry*. 1996;60:628–633.
DOI: 1136/jnnp.60.6.628
25. Borjesson-Hanson A, Edin E, Gislason T, Skoog I. The prevalence of dementia in 95 year olds. *Neurology*. 2004;63:2436–2438.
26. Shaji S, Bose S, Verghese A. Prevalence of dementia in an urban population in Kerala, India. *Br J Psychiatry*. 2005;186: 136–140.
27. Ott A, Breteler MM, van Harskamp F, Claus JJ, Cammen TJ van der, Grobbee DE, Hofman A. Prevalence of Alzheimer's disease and vascular dementia: Association with education. The Rotterdam study. *BMJ*. 1995;310:970–973.
28. Karp A, Kareholt I, et al. Relation of education and occupation-based socioeconomic status to incident Alzheimer's disease. *Am J Epidemiology*. 2004;159:175–83.
29. Roy J, Sugathan TN. Kerala Suvey of Alzheimer's & related disorders. ICMR Project; 1999.
30. Katzman R, Aronson M, Fuld P, et al. Development of dementing illnesses in an 80-year-old volunteer cohort. *Ann Neurol*. 1989;25:317–24.
31. Wang P-N, Wang S-J, Hong C-J, et al. Risk factors for Alzheimer's disease: A case-control study. *Neuroepidemiology*. 1997;16:234–40.
32. Launer LJ, Andersen K, Dewey ME, et al. Rates and risk factors for dementia and Alzheimer's disease: Results from EURODEM pooled analyses. *Neurology*. 1999;52:78–84.
33. Sun MK, Alkon DL. Links between Alzheimer's disease and diabetes. *Drugs Today (Barc)*. 2006;42:481–932.
34. Forette F, Boller F. Hypertension and the risk of dementia in the elderly. *Am J Med*. 1991;90:14S–9S.
35. Posner HB, Tang MX, Luchsinger J, et al. The relationship of hypertension in the elderly to AD, vascular dementia, and cognitive function. *Neurology*. 2002;58: 1175–81.
36. The Canadian Study of Health and Aging: Risk factors for Alzheimer's disease in Canada. *Neurology*. 1994;44:2073–80.
37. Craft S. Insulin resistance and Alzheimer's disease pathogenesis: Potential mechanisms and implications for treatment. *Curr Alzheimer Res*. 2007;4: 147–52.
38. Lye TC, Shores EA. Traumatic brain injury as a risk factor for Alzheimer's disease: A review. *Neuropsychol Rev*. 2000;10:115–29.
39. Fleminger S, Oliver DL, Lovestone S, et al. Head injury as a risk factor for Alzheimer's disease: The evidence 10 years on; a partial replication. *J Neurosurgery Psychiatry*. 2003;74:857–62.
40. Merchant C, Tang MX, Albert S, et al. The influence of smoking on the risk of Alzheimer's disease. *Neurology*. 1999;52: 1408–12.

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