# Smoking and Cognitive Impairment Among Older Persons in Malaysia

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#### Abstract

**Introduction:** Previous studies have shown conflicting results on the association between smoking and cognitive function. This study aims to examine the relationship of smoking with cognitive function. **Methodology:** Data for the study, consisting of 2553 older adults aged 60 years and older, were drawn from a nationwide household survey entitled "Determinants of Wellness among Older Malaysians: A Health Promotion Perspective" conducted in 2010. **Results:** Current smokers had lower rates of cognitive impairment compared to never smokers (17.4% vs 25.9%), while cognitive function in former or ex-smokers was almost similar to that of the never smokers. Findings from multiple logistic regression analysis showed that current smokers were 37% less likely to be cognitively impaired, compared to the never smokers (odds ratio [OR] = .63; 95% confidence interval [CI]: .46-.86) while controlling for potential confounders. No difference in cognitive function was observed between former smokers and never smokers (OR = .94; 95% CI: .71-1.25). **Conclusion:** Although the findings indicated a negative association between cigarette smoking and cognitive impairment, we are unable to conclude whether this relationship is causal or affected by other unmeasured confounding factors, especially survival bias.

#### Keywords

aged, cigarette smoking, cognitive impairment, Malaysia

## Introduction

With the rapidly aging global population, cognitive impairment in old age is a growing worldwide concern.<sup>1,2</sup> Since there is no absolute cure for cognitive disorders,<sup>3</sup> a growing body of research has been focusing on identifying modifiable risk factors contributing to the condition. In light of this, one of the risk factors that has been widely studied is cigarette smoking. Although there is evidence to support that cigarette smoking has considerable adverse effects on health and that smoking contributes to many age-related diseases,4-6 studies have produced conflicting findings on the association between smoking and dementia.7 Observational studies suggest that smoking might be protective against Alzheimer's disease (AD),<sup>8-10</sup> whereas longitudinal studies have found that smokers have the same<sup>11-13</sup> or increased risk of dementia and AD.<sup>14-16</sup> For example, the findings from 2 meta-analyses of longitudinal studies concluded by Anstey et al<sup>16</sup> as well as Peters et al<sup>17</sup> have shown that current smoking is associated with an increased risk of dementia.

Although majority of the previous prospective studies have found that smoking increases the risk of dementia, surprisingly, the findings from a recent longitudinal study conducted by Wang and his colleagues<sup>18</sup> indicated that smokers were less likely to develop cognitive impairment compared to never smokers, after controlling for age, education, hypertension, diabetes, heart disease, and stroke at baseline. The study suggested that smoking might have protective effect for cognitive function.

In sum, a review of research focusing on the association between smoking and cognitive function shows apparently conflicting results, especially between cross-sectional and longitudinal studies. Several studies have found that smoking improves cognitive function; however, some other studies have found that smoking is associated with increased risk of dementia. Therefore, the impact of smoking on cognitive performance needs more clarification.<sup>18</sup> The current crosssectional study aimed to examine the association between smoking and cognitive function among community-dwelling elderly individuals.

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# Methodology

Data for this cross-sectional study were drawn from a nationally representative household survey entitled "Determinants of Wellness among Older Malaysians: A Health Promotion Perspective" conducted in 2010. The methodology of the study has been previously published elsewhere.<sup>19</sup> Briefly, the survey used a 2-stage proportional random sampling technique to obtain a sample of 2562 older adults aged 60 years and older, with a response rate of 77%. The primary sampling units were Census enumeration blocks. The secondary sampling units were private households randomly selected from the list of all enumerated households in each block. All selected respondents were interviewed by trained enumerators. The final sample size after data cleaning was 2553 respondents.

## Ethics and Approval

The study was approved by the Ministry of Health, Malaysia, and was in compliance with the Declaration of Helsinki and the World Medical Association guidelines. After providing a disclosure statement about the purpose of the survey, oral informed consent was obtained from all respondents before commencing the interview.

# Measures

#### Cognitive Impairment

The main outcome variable was cognitive impairment, measured using with the Mini-Mental State Examination (MMSE). The MMSE assesses 5 areas of cognitive function including orientation, attention, calculation, language, and recall. The cutoff point 18 of 19 was used for detecting cognitive impairment in illiterate respondents and 24 of 25 was used for the educated.<sup>20,21</sup>

## History of Smoking

Respondents were asked whether they have ever smoked and whether they are still smoking. Based on the responses, respondents were classified into 3 main categories: never smokers, current smokers, and former smokers.

# Chronic Medical Conditions

Chronic medical conditions (CMCs) were assessed using a checklist of self-reported chronic health problems including hypertension, heart disease, stroke, diabetes, cancer, visual problems, hearing problems, gastritis, asthma, kidney disease, joint pain (arthritis), and tuberculosis during the previous 12 months. The number of chronic medical conditions was categorized into 3 categories: zero, 1 to 2, and 3 or more.

#### Sociodemographic Factors

Sociodemographic characteristics, including age, education (in years), gender, and household income, were included in the analysis.

### Statistical Analysis

The data were analyzed using SPSS version 21. A 2-step hierarchical logistic regression model was used to determine unique effect of smoking on cognitive impairment after controlling for potential confounders. Hosmer-Lemeshow tests were used to determine goodness of fit for the hierarchical logistic regression models. The P value criterion used for evaluating statistical significance was .05. Smoking status was entered in the first block. Sociodemographic factors and health factors were included in the second model, namely the variables on age, gender, educational attainment, household income, and CMCs.

# Results

Table 1 presents the smoking status and demographic characteristics of the study respondents by their cognitive function. As can be seen from Table 1, 55% of the 2553 respondents who participated in the survey were women, and 40% of the respondents had no formal education. Less than one-fifth (15.9%) of the study participants indicated that they were current smokers, 17% were former smokers, and 67.1% reported having never smoked. The prevalence of cognitive impairment among current smokers was 17.4%. The former smokers and never smoked had a similar prevalence of cognitive impairment (24.5% vs 25.9%). A 1-way analysis of variance was used to test for differences in cognitive function among the 3 groups. Since the assumption of homogeneity of variance was violated (Levene Statistic = 14.94,  $P \leq .05$ ), the Brown Forsythe F ratio was reported. There was a significant difference in cognitive function among respondents by smoking history,  $F_{2, 1248.13} =$ 20.84, P < .001. Tukey post hoc comparisons of the 3 groups indicated that the mean cognitive function score of the current smokers (M = 25.86, standard deviation [SD] = 4.68) was significantly higher than the former smokers (M = 24.43, SD = 5.56) and never smokers (M = 23.99,SD = 5.78).

The results of chi-square analyses presented in Table 1 showed significant association between cognitive impairment with smoking status ( $\chi^2 = 12.84$ , P < .001), gender ( $\chi^2 = 9.21$ , P < .01), age ( $\chi^2 = 58.07$ , P < .001), household income ( $\chi^2 = 46.83$ , P < .001), CMCs ( $\chi^2 = 17.10$ , P < .001), and educational attainment ( $\chi^2 = 37.72$ , P < .001).

A series of chi-square analyses were also performed to examine the relationships between the sociodemographic variables and smoking status (see Table 2). The findings revealed significant associations between smoking status, gender ( $\chi^2 = 742.58$ , P < .001), marital status ( $\chi^2 = 97.99$ ,

Table I.	Distribution	of Stud	y Variables b	y Cognitive	Impairment. <sup>a</sup>

		Total		Noncognitively Impaired		Cognitively Impaired		
Variable	Category	n	%	n	%	n	%	$\chi^2$
Smoking status	Never smokers	1713	67.1	1269	65.7	444	71.5	12.84 <sup>b</sup>
6	Former smokers	433	17.0	327	16.9	106	17.1	
	Current smokers	407	15.9	336	17.4	71	11.4	
Gender	Male	1150	45.0	903	46.7	247	39.8	9.21 <sup>b</sup>
	Female	1403	55.0	1029	53.3	374	60.2	
Age	<68	1219	47.7	1005	52.0	214	34.5	58.07 <sup>c</sup>
0	>68	1334	52.3	927	48.0	407	65.5	
Household income, RM	<300	769	30.1	522	27.0	247	39.8	46.83°
	300-800	1144	44.8	876	45.3	268	43.2	
	>800	640	25.1	534	27.6	106	17.1	
CMC	No CMC	466	18.3	376	19.5	90	14.5	17.10 <sup>c</sup>
	I-2 CMC	1320	51.7	1013	52.4	307	49.4	
	3+ CMCs	767	30.0	543	28.1	224	36.1	
Education	No Formal	1022	40.0	732	37.9	290	46.7	37.72°
	Primary	1155	45.2	871	45.I	284	45.7	
	Secondary and tertiary	376	14.7	329	17.0	47	7.57	

Abbreviations: CMC, chronic medical condition; RM: Ringgit Malaysia.

<sup>b</sup>P < .01.

<sup>c</sup>P < .001.

#### Table 2. Distribution of Study Variables by Smoking Status.<sup>a,b</sup>

		Never Smokers		Past Smoker		Current Smokers		
Variable	Category	n	%	n	%	n	%	$\chi^2$
Gender	Male	450	26.3	353	81.5	347	85.3	742.58°
	Female	1263	73.7	80	18.5	60	14.7	
Age	<68	822	48.0	190	43.9	207	50.9	4.22
0	>68	891	52.0	243	56. I	200	49.1	
Household Income	<300	557	32.5	101	23.3	111	27.3	24.20 <sup>c</sup>
	300-800	762	44.5	191	44.I	191	46.9	
	>800	394	23.0	141	32.6	105	25.8	
CMC	No CMC	301	17.6	62	14.3	103	25.3	27.38 <sup>c</sup>
	I-2 CMCs	877	51.2	227	52.4	216	53.I	
	3+ CMCs	535	31.2	144	33.3	88	21.6	
Education	No formal	755	44.1	145	33.5	122	30.0	36.81 <sup>c</sup>
	Primary	725	42.3	214	49.4	216	53.I	
	Secondary and Tertiaryt	233	13.6	74	17.1	69	17.0	

Abbreviation: CMCs, chronic medical conditions.

<sup>c</sup>P < .001.

P < .001), household income ( $\chi^2 = 24.20, P < .001$ ), CMCs ( $\chi^2 = 27.38, P < .001$ ), and educational attainment ( $\chi^2 = 36.81, P < .001$ ).

## Hierarchical Logistic Regression

The first block (smoking history) was significant according to the model chi-square statistics. Current smokers had a lower risk of cognitive impairment than never smokers (odds ratio [OR] = .60; 95% confidence interval [CI], .46-.80). The findings from block 2 also revealed a significant model where smoking status remained a significant factor that contributed toward cognitive impairment at P = .01 while controlling for potential confounders such as age, gender, educational attainment, household income, and chronic medical conditions. Table 3 showed that there are no significant difference between former smokers and never smokers (OR = .94, 95% CI: 0.71-1.25).

 $<sup>^{</sup>a}P \leq .05.$ 

 $<sup>^{</sup>a}P \leq .05.$ 

<sup>&</sup>lt;sup>b</sup>P < .01.

Tal	ble	3. 3	Summary	of	Hierarc	hical	Logistic	Regression	1 Model.
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			-	-			
		Block I		Block 2			
		95%	6 CI		95% CI		
Variable	OR	Lower	Upper	OR	Lower	Upper	
Smoking status							
Past smoker	0.93	0.73	1.18	0.94	0.71	1.25	
Current smoker	0.60 <sup>a</sup>	0.46	0.8	0.63 <sup>b</sup>	0.46	0.86	
Age				1.82ª	1.49	2.22	
Female				I	0.79	1.26	
Education (Ref: no f	ormal)						
Primary				1.14	0.92	1.4	
Secondary and				0.63 <sup>c</sup>	0.43	0.91	
tertiary							
Household Income	(Ref: <3	00)					
300-800				0.7 <sup>b</sup>	0.57	0.87	
>800				0.53ª	0.4	0.7	
CMCs (Ref: no CMC	C)						
I-2 CMCs				1.2	0.92	1.57	
3+ CMCs				1.45°	1.09	1.94	
Model statistics							
$\chi^2$	13.61			123.66			
df	2			10			
Model significance	<0.001			<0.001			

Abbreviations: CI, confidence interval; CMCs, chronic medical conditions; OR, odds ratio.

<sup>b</sup>P < .01. <sup>c</sup>P ≤ .05.

## Discussion

The prevalence of cigarette smoking among older Malaysians aged 60 years and older in the present study was found to be 15.9% (30.2% among males and 4.3% among females), similar to the national prevalence rate of smoking among older adults.<sup>22</sup> The study provided evidence of a lower rate of current smoker status among cognitively impaired respondents compared to the respondents without cognitive impairment (11.1% vs 17%).

The main purpose of this cross-sectional study was to examine the association between smoking and cognitive function. Consistent with previous studies of similar research design,<sup>18,23</sup> we found an inverse relationship between smoking and cognitive impairment. The findings are inconsistent with a growing body of empirical evidence, particularly from longitudinal studies, which showed smoking increases the odds of cognitive impairment.<sup>16,24-29</sup>

The finding that showed no significant difference in cognitive function between former smokers and never smokers was consistent with several past studies.<sup>28,30</sup> However, there are other studies which linked smoking history to cognitive function and found that former smokers have better cognitive scores than never smokers.<sup>18,31,32</sup> For example, the findings from a prospective study among older Taiwanese respondent indicated that former smokers had a lower risk of cognitive impairment compared to never smokers, after controlling for age, education, diabetes, hypertension, stroke, and heart disease.<sup>18</sup> Conversely, the results of other studies provided evidence to the contrary where former smokers have a higher rate of cognitive decline.<sup>16,29,33</sup>

Although the exact mechanisms by which cigarette smoking contributes to dementia have not yet been completely understood, it is believed that smoking damages the cardiovascular system and causes oxidative stress, the conditions that may increase the risk of dementia and AD. Smoking can increase the risk of AD and dementia through the cardiovascular system.<sup>29</sup> There was evidence that smoking is also a risk factor for hypertension.<sup>34,35</sup> It was found that hypertension is associated with an increased risk of Alzheimer's disease and dementia through cerebrovascular pathology and Alzheimer's disease pathology.<sup>16,17,36</sup>

Oxidative stress is another mechanism that may explain the negative effect of smoking on cognitive function. Oxidative stress caused by cigarette smoking damages cells in the blood vessels and results in narrowing of the arteries and reducing cerebral blood flow. Consequently, reduced cerebral perfusion may account for cognitive impairment.<sup>24,26</sup> Recent studies showed that oxidative stress plays a significant role in the onset and development of Alzheimer's disease.<sup>37-39</sup>

Another possible mechanism that may account for the contribution of smoking to cognitive function is through lifestyle factors. Studies have shown that cigarette smoking is associated with increased consumption of alcohol,<sup>40,41</sup> unhealthy body mass index,<sup>42,43</sup> and low physical activity,<sup>44,45</sup> conditions that are considered as leading causes of cognitive impairment.46,47 Nonphysiological mechanism may also explain the association between cigarettes smoking and cognitive impairment. First, population-based studies have found an inverse association between socioeconomic status (SES) and smoking behavior, whereas people with lower SES are more likely to become smokers.<sup>48,49</sup> Second, several studies have shown that socioeconomic factors may have a role in dementia etiology. 50-52 Therefore, the link between low SES and smoking habits may partly explain why smokers may be at greater risk of cognitive impairment.

In contrast, the potential biological protective effects of smoking on dementia has been attributed to nicotine.53,54 Nicotine can improve short-term cognitive performance and inhibits amyloid formation.<sup>16</sup> It stimulates receptors in the brain that are important for thinking and memory.<sup>55,56</sup> Another explanation for negative association between cigarette smoking and cognitive impairment could be owing to the fact that cigarette smokers die at younger ages than nonsmokers, thus creating a survivorship bias. Consequently, fewer smokers are alive at the ages when dementia symptoms typically onset.<sup>57</sup> Therefore, lower rates of dementia among smokers may have little or nothing to do with any protective quality of smoking and actually be attributable to smokers dying early from other diseases before the onset of dementia.<sup>58</sup> For example, in their study, Sabia and colleagues examined whether the smokingcognition association is underestimated owing to premature mortality among smokers and found that current smokers had

 $<sup>^{</sup>a}P < .001.$ 

a higher risk of dying during follow-up compared to never smokers, after controlling for age, socioeconomic status, and marital status among men and women.<sup>57</sup>

Although, our study benefits from a large representative sample of Malaysian older adults 60 years and older, its crosssectional nature limits causal conclusions. Another important limitation that should be highlighted is that smoking assessment was solely based on self-report. Some studies indicate that respondents tend to underreport socially undesirable behaviors, such as tobacco use, which may result in the underestimation of the association between smoking and cognitive function. The last limitation that should be acknowledged is related to the use of MMSE. Although the MMSE is widely used as an effective screening instrument for cognitive impairment, it relies heavily on the verbal response, reading, and writing. Therefore, nonformal educated respondents may perform poorly in spite of being cognitively intact.<sup>59</sup>

# Conclusion

The findings from the present cross-sectional research are in accordance with some previous studies which showed that cigarette smoking may be associated with a lower risk of cognitive impairment. It should be acknowledged that from the present study, we are unable to conclude whether the negative association between cigarette smoking and cognitive impairment is causal or due to other unmeasured confounding factors that require further study to identify the biopsychosocial mechanisms linking cigarette smoking to cognitive function.

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#### References

- Momtaz YA, Hamid TA, Yusoff S, Ibrahim R. Do depression and educational attainment mediate the association between ethnicity and dementia? *Gerontology*. 2012;59(3):206-212.
- Formiga F, Ferrer A, Chivite D, et al. Predictors of cognitive decline in 85-year-old patients without cognitive impairment at baseline: 2-year follow-up of the Octabaix Study. *Am J Alzheimers Dis Other Dement*. 2013 2013;28(2):147-153.
- 3. News Briefs. Analyst insight: Alzheimer's efforts shift from cure to prevention: Emerging biomarkers, and possible ties to

diabetes. Am J Alzheimers Dis Other Dement. 2012;27(8): 640-651.

- Jee SH, Suh I, Kim IS, Appel LJ. Smoking and atherosclerotic cardiovascular disease in men with low levels of serum cholesterol. *JAMA*. 1999;282(22):2149-2155.
- Gorelick PB, Sacco RL, Smith DB, et al. Prevention of a first stroke. JAMA. 1999;281(12):1112-1120.
- Ford AB, Mefrouche Z, Friedland RP, Debanne SM. Smoking and cognitive impairment: A population-based study. J Am Geriatr Soc. 1996;44(8):905-909.
- Almeida OP, Hulse GK, Lawrence D, Flicker L. Smoking as a risk factor for Alzheimer's disease: contrasting evidence from a systematic review of case-control and cohort studies. *Addiction*. 2002;97(1):15-28.
- Tyas SL. Are tobacco and alcohol use related to Alzheimer's disease? A critical assessment of the evidence and its implications. *Addiction Biol.* 1996;1(3):237-254.
- Lee PN.Smoking and Alzheimer's disease: A review of the Epidemiological evidence. *Neuroepidemiology*. 1994;13(4): 131-144.
- Fratiglioni L, Wang HX. Smoking and Parkinson's and Alzheimer's disease: Review of the epidemiological studies. *Beha*vioural Brain Res. 2000;113(1):117-120.
- Brayne C, Gill C, Huppert FA, et al. Vascular risks and incident dementia: results from a cohort study of the very old. *Dement Geriatr Cogn Disord*. 1998;9(3):175-180.
- 12. Broe GA, Creasey H, Jorm AF, et al. Health habits and risk of cognitive impairment and dementia in old age: a prospective study on the effects of exercise, smoking and alcohol consumption. Aust N Z J Public Health. 1998;22(5):621-623.
- Doll R, Peto R, Boreham J, Sutherland I. Smoking and dementia in male British doctors: Prospective study. *BMJ*. 2000; 320(7242):1097.
- Merchant C, Tang MX, Albert S, Manly J, Stern Y, Mayeux R. The influence of smoking on the risk of Alzheimer's disease. *Neurology*. 1999;52(7):1408-1408.
- Ott A, Slooter AJC, Hofman A, et al. Smoking and risk of dementia and Alzheimer's disease in a population-based cohort study: The Rotterdam study. *Lancet*. 1998;351(9119): 1840-1843.
- Anstey KJ, von Sanden C, Salim A, O'Kearney R. Smoking as a risk factor for dementia and cognitive decline: A metaanalysis of prospective studies. *Am J Epidemiol.* 2007; 166(4):367-378.
- Peters R, Poulter R, Warner J, Beckett N, Burch L, Bulpitt C. Smoking, dementia and cognitive decline in the elderly, a systematic review. *BMC Geriatr.* 2008;8(1):36.
- Wang CC, Lu TH, Liao WC, et al. Cigarette smoking and cognitive impairment: A 10-year cohort study in Taiwan. *Arch Gerontol Geriatr.* 2010;51(2):143-148.
- Momtaz YA, Hamid TA, Ibrahim R, Akahbar SAN. Racial and socioeconomic disparities in sexual activity among older married Malaysians. *Arch Gerontol Geriatr.* 2014;58(1):51-55.
- LourencoI RA, Vera RP. Mini-mental state examination: psychometric characteristics in elderly outpatients. *Rev Saude Publica*. 2006;40(4):712-719.

- Momtaz YA, Hamid TA, Ibrahim R. The impact of mild cognitive impairment on sexual Activity. *Am J Alzheimers Dis Other Dement.* 2013;28(8):759-762.
- Lim HK, Ghazali SM, Kee CC, et al. Epidemiology of smoking among Malaysian adult males: prevalence and associated factors. *BMC Public Health*. 2013;13(1):8.
- Levin ED, McClernon FJ, Rezvani AH. Nicotinic effects on cognitive function: behavioral characterization, pharmacological specification, and anatomic localization. *Psychopharmacol*ogy. 2006;184(3-4):523-539.
- Rusanen M, Kivipelto M, Quesenberry CP Jr, Zhou J, Whitmer RA. Heavy smoking in midlife and long-term risk of Alzheimer disease and vascular dementia. *Arch Intern Med.* 2011;171(4): 333-339.
- Gons RAR, van Norden AGW, de Laat KF, et al. Cigarette smoking is associated with reduced microstructural integrity of cerebral white matter. *Brain*. 2011;134(7):2116-2124.
- Collins N, Sachs-Ericsson N, Preacher KJ, Sheffield KM, Markides K. Smoking increases risk for cognitive decline among community-dwelling older Mexican Americans. *Am J Geriatr Psychiatry*. 2009;17(11):934-942.
- Swan GE, Lessov-Schlaggar CN. The effects of tobacco smoke and nicotine on cognition and the brain. *Neuropsychol Rev.* 2007;17(3):259-273.
- Nooyens ACJ, van Gelder BM, Verschuren WMM. Smoking and cognitive decline among middle-aged men and women: The Doetinchem Cohort Study. *Am J Public Health*. 2008;98(12): 2244-2250.
- Mons U, Schottker B, Muller H, Kliegel M, Brenner H. History of lifetime smoking, smoking cessation and cognitive function in the elderly population. *Eur J Epidemiol.* 2013;28(10): 823-831.
- Galanis DJ, Petrovitch H, Launer LJ, Harris TB, Foley DJ, White LR. Smoking history in middle age and subsequent cognitive performance in elderly Japanese-American men: the Honolulu-Asia Aging Study. *Am J Epidemiol.* 1997;145(6): 507-515.
- Sabia S, Elbaz A, Dugravot A, et al. Impact of smoking on cognitive decline in early old age: The Whitehall II cohort study. *Arch Gen Psychiatry*. 2012;69(6):627-635.
- Richards M, Jarvis MJ, Thompson N, Wadsworth MEJ. Cigarette smoking and cognitive decline in midlife: evidence from a prospective birth cohort study. *Am J Public Health*. 2003;93(6): 994-998.
- Ott A, Andersen K, Dewey ME, et al. Effect of smoking on global cognitive function in nondemented elderly. *Neurology*. 2004; 62(6):920-924.
- Halperin RO, Gaziano JM, Sesso HD. Smoking and the risk of incident hypertension in middle-aged and older men. *Am J Hypertens*. 2008;21(2):148-152.
- Bonita R.Cigarette smoking, hypertension and the risk of subarachnoid hemorrhage: A population-based case-control study. *Stroke*. 1986;17(5):831-835.
- Knopman DS. Hypertension and late-life dementia: a real link? Neurology. 2009;72(20):1716-1717.

- Chong ZZ, Li F, Maiese K. Stress in the brain: novel cellular mechanisms of injury linked to Alzheimer's disease. *Brain Res Rev.* 2005;49(1):1-21.
- Khanna A, Guo M, Mehra M, Royal III W. Inflammation and oxidative stress induced by cigarette smoke in Lewis rat brains. *J Neuroimmunol.* 2013;254(1):69-75.
- Ho YS, Yang X, Yeung SC, et al. Cigarette smoking accelerated brain aging and induced pre-Alzheimer-like neuropathology in rats. *PloS One*. 2012;7(5):e36752.
- Burns BE, Proctor WR. Cigarette smoke exposure greatly increases alcohol consumption in adolescent C57BL/6 mice. *Alcohol Clin Exp Res.* 2013;37(s1):E364-E372.
- Watten RG. Smokers and non-smokers: differences in alcohol consumption and intake of other health-related substances in Norway: a general population study. *Eur J Public Health*. 1999;9(4):306-308.
- 42. Sneve M, Jorde R. Cross-sectional study on the relationship between body mass index and smoking, and longitudinal changes in body mass index in relation to change in smoking status: the Tromso Study. *Scand J Public Health*. 2008;36(4): 397-407.
- Chiolero A, Faeh D, Paccaud F, Cornuz J. Consequences of smoking for body weight, body fat distribution, and insulin resistance. *Am J Clin Nutr.* 2008;87(4):801-809.
- Furlanetto KC, Mantoani LC, Bisca G, et al. Reduction of physical activity in daily life and its determinants in smokers without airflow obstruction. *Respirology*. 2014;19(3):369-375.
- 45. Campbell Jenkins B, Sarpong D, Addison C, et al. Joint effects of smoking and sedentary lifestyle on lung function in African Americans: The Jackson Heart Study Cohort. *Int J Environ Res Public Health.* 2014;11(2):1500-1519.
- Sofi F, Valecchi D, Bacci D, et al. Physical activity and risk of cognitive decline: A meta-analysis of prospective studies. *J Intern Med.* 2011;269(1):107-117.
- de Bruijn RFAG, Schrijvers EMC, de Groot KA, et al. The association between physical activity and dementia in an elderly population: The Rotterdam Study. *Eur J Epidemiol.* 2013; 28(3):277-283.
- Hiscock R, Bauld L, Amos A, Fidler JA, Munafo M. Socioeconomic status and smoking: a review. *Ann N Y Acad Sci.* 2012; 1248(1):107-123.
- Parrish A, Mason C. Low Socioeconomic Status and Cancer Prevention in the American Cancer Society Great West Division. Washington, DC: Health Promotion Research Center; 2013.
- 50. Russ TC, Stamatakis E, Hamer M, Starr JM, Kivimäki M, Batty GD. Socioeconomic status as a risk factor for dementia death: individual participant meta-analysis of 86 508 men and women from the UK. *Br J Psychiatry*. 2013;203(1): 10-17.
- Yaffe K, Falvey C, Harris TB, et al. Effect of socioeconomic disparities on incidence of dementia among biracial older adults: Prospective study. *BMJ*. 2013;347:f7051.
- 52. Hamid TA, Krishnaswamy S, Abdullah SS, Momtaz YA. Sociodemographic risk factors and correlates of dementia in

older Malaysians. Dement Geriatr Cogn Disord. 2011;30(6): 533-539.

- White HK, Levin ED. Four-week nicotine skin patch treatment effects on cognitive performance in Alzheimer's disease. *Psychopharmacology*. 1999;143(2):158-165.
- Levin ED. Nicotinic systems and cognitive function. *Psychopharmacology*. 1992;108(4):417-431.
- Newhouse PA, Potter A, Singh A. Effects of nicotinic stimulation on cognitive performance. *Curr Opin Pharmacol.* 2004;4(1): 36-46.
- Rezvani AH, Levin ED. Cognitive effects of nicotine. *Biol Psychiatry*. 2001;49(3):258-267.
- 57. Sabia S, Marmot M, Dufouil C, Singh-Manoux A. Smoking history and cognitive function in middle age from the white-hall ii study. *Arch Intern Med.* 2008;168(11):1165-1173.
- Debanne SM, Rowland DY, Riedel TM, Cleves MA. Association of Alzheimer's disease and smoking: The case for sibling controls. J Am Geriatr Soc. 2000;48(7):800-806.
- Kurlowicz L, Wallace M. The mini mental state examination (MMSE). J Gerontol Nurs. 1999;25(5):8-9.