How do our decisions to smoke and drink in midlife affect our cognitive performance in later life? Findings from the 1946 British Birth Cohort

Martina Vňuková[1], Marcus Richards[2] and Dorina Cadar[3*]

[1]Department of Psychiatry - First Faculty of Medicine Charles University and General University Hospital, Czech Republic

[2]MRC Unit for Lifelong Health and Ageing at University College London, UK

[3]Research Department of Behavioural Sciences and Health, University College London, London, UK

*Corresponding author: Dorina Cadar, Research Associate in Dementia, Department of Behavioural Health Sciences, University College London, Torrington Place London, Tel: 02076795969; E-mail: d.cadar@ucl.ac.uk

Abstract

Background: There is not a clear understanding of the potential time-period windows for lifestyle interventions. This study examined how smoking and harmful drinking across early midlife affect cognitive performance in later life.

Methods: Data is from Medical Research Council National Survey of Health and Development (NSHD). Cognitive abilities were measured at age 60-64. Information about alcohol consumption was collected via food diaries at multiple time points across life (ages 36, 43, 53 and 60-64). Information about smoking was collected via interviews and questionnaires at ages 20, 25, 31, 36, 43, 53 and 60-64. Multivariable logistic regression was used, adjusting for gender, childhood cognition at age 8, education and socioeconomic status.

Findings: Drinking in moderation across midlife appears to be protective against poor memory in later life (OR=0.86, 95% CI (0.63-1.16)). In contrast, harmful drinking at 43 and 53 years was associated with higher odds of poor memory (OR=1.36, 95% CI (0.79-2.33)), (OR=1.26, 95% CI (0.65-2.43)). Drinking heavily, particularly at age 43, was also associated with higher odds of slow search speed at the same age (OR=1.66, 95% CI (1.01-2.76)). An increase in the number of smoking pack-years was associated with low memory (OR=2.17, 95% CI (1.33-3.54)) and slow search speed (OR=1.65, 95% CI (1.03-2.64)).

Interpretation: These results may be suggesting that intervention may be more beneficial in the decades preceding clinical manifestation of neuropathological burden.

Keywords: cognitive performance, cognitive impairment, aging, smoking, alcohol, life-course, birth cohort, longitudinal analyses

1. Introduction

World population is slowly aging, those aged 85 and older being the group with the fastest growing rate [1]. Older age is commonly associated with dementia; current estimates predict that the number of people affected by dementia will double every 20 years and by 2040 the estimated number of affected people will reach 81.1 million [2]. Previous research indicated an association between dementia and modifiable risk factors such as alcohol consumption [3]. It has been suggested that leading a physically active and an intellectually challenging life may have a positive impact on our well-being [4].

Cadar et al. assessed the role of lifestyle behaviors on the 20-year cognitive decline and found an association between heavy smoking and faster cognitive decline in tests of memory and visual search [5]. Similarly, Van Gelder et al. showed that even at old age, cognitive decline may be postponed by medium-low intensity activities and if duration or intensity are decreased even stronger cognitive decline may result [6]. In Whitehall II Study, similar findings were reached. It is not only the number of unhealthy behaviors but also the duration that is associated with cognitive functions in later life [7]. Despite various recommendations of maintaining healthy lifestyles, very few people meet these proposed guidelines [8].

There is scarce and mixed evidence about the relationship between alcohol consumption and cognitive performance. Some studies show a protective role of moderate alcohol consumption; however, there is a certain amount of discrepancy among these assumptions. A common belief is that the association between alcohol and cognitive functioning take the form of a J-curve which demonstrates how both extremes; non-drinking and alcohol abuse have an adverse impact on cognitive functioning. For example, Antilla et al. found that participants who either did not drink any alcohol at midlife or often drunk heavily, were twice as likely to have mild cognitive impairment in old age compared to those who drank alcohol in moderation [9]. A positive effect of moderate drinking was also found by Elias et al. ; they concluded that women who consumed alcohol in moderation demonstrated better performance in many cognitive domains when compared to non-drinkers [10]. In the case of men, better performance was observed when they drank within the range of recommended daily units of alcohol; 4-8 drinks a day [11]. Park and colleagues also highlighted gender differences in smoking and alcohol consumption on cognitive functioning [12]. Other studies conducted by Luchsinger et al. or Peters et al. point to the possibility of certain protective effects of moderate alcohol consumption [13,14].

In contrast, there is also evidence demonstrating a strong association between alcohol abuse and faster cognitive decline or earlier onset of dementia [15-18]. Alcohol-related dementia accounts for the second-most common cause of dementia among elderly. Furthermore, Cadar and colleagues highlighted the difference between short-term and long-term effects of alcohol on cognition and the importance of education [19].

Smoking is yet another risk factor associated with many health-related diseases such as cardiovascular disease and dementia [20]. History of smoking was also found to be related to preclinical changes in the brain, accelerated risk of cognitive decline and increased risk of dementia. Multiple studies have shown that smoking is associated with a reduction of grey matter volume [21-23]. Tyas et al. suggest that the number of cigarettes smoked is directly associated with the risk of AD [24]. Starr et al. found adverse effects of smoking on cognition (memory) [25]. In the 1946 British Birth Cohort, Richards et al. have shown that heavy smoking is associated with cognitive impairment, as well as cognitive decline in midlife [26]. The association between smoking and increased risk of cognitive decline as well as dementia has been confirmed in several other studies [20,24,27].

Both smoking and heavy alcohol intake are lifestyle behaviors that carry a high risk of increased cognitive impairment and mortality. A review by Lee et al. reinforces the adverse effects of smoking on dementia and AD, as well as the association between alcohol intake and increased risk of dementia [28]. However, there is also evidence suggesting that moderate wine consumption may have protective effects against Alzheimer's disease [29]. In a review, it was highlighted that moderate wine consumption was considered to have protective effects [30]. The same report indicated that in contrast, smoking increases the risk of dementia in older age. In a longitudinal study of 1,292 American men of Japanese ancestry, current and past smoking were associated with non-survival, rather than unhealthy survival, while midlife drinking (more than three alcohol units per day) was associated with both non-survival and unhealthy survival [31]. Furthermore, Zhou and colleagues assessed both smoking and drinking and their effects on cognition and saw a strong association between smoking and cognitive impairment as well as the association between drinking and cognitive impairment [32]. Richards and Hatch also highlight the importance of life-course approaches to the understanding of mental aging and risk factors [33]. Since both smoking and alcohol consumption are modifiable lifestyle factors, it is important to reassess their roles on the level of cognitive performance and impairment, given the higher risk of dementia in those exhibiting these declines.

The aim of this study was to investigate the impact of unhealthy lifestyle behaviors (heavy smoking and heavy drinking) in early midlife (ages 36 to 43) on cognitive impairment at ages (60 to 64) in the MRC National Survey of Health and Development (NSHD). The specific objectives were to assess the potential cognitive impairment at age 60-64 and to investigate the effects of heavy drinking and heavy smoking on cognitive impairment. Furthermore, this work examined the clustering effects of smoking and drinking across midlife on cognitive impairment. The associated hypothesis was that heavy tobacco use and harmful drinking in early midlife would negatively affect cognitive abilities in later life. Results of this study should be able to set out the implications for public health policy.

2. Methods

2.1. Participants

Data from Medical Research Council (MRC) National Survey of Health and Development (NSHD) were used. This cohort consisted of 5362 children born in one week of March 1946 in England, Scotland and Wales. Since then, there have been 25 waves of data collection. Information about socio-demographic characteristics, medical, cognitive and psychological functioning was collected via interviews, examinations and self-report questionnaires [34].

2.2. Study variables

Cognitive abilities were measured at age 60-64 using memory and speed tasks. Short-term memory was assessed with a 15-item word list, and speed was assessed with a time letter search task. For each of these two categories, the scores were divided into tertiles (low, medium and high). Medium and high categories have been merged into one group of higher scores and used as a reference category in the models, in comparison to low scores.

Alcohol at age: 36, 43, 53, 60-64. Alcohol consumption was measured via food diaries (over five days) and verbal recall (two days) during interviews. Subsequently, averages of recorded scores were derived for each wave of data collection. Daily averages were classified into four categories, according to the guidelines by Science and Technology Committee (2011).

The categories were: *non-drinker* (0 units of alcohol), *low – moderate drinker* (<3 units - males/<2 units - females), *heavy drinker* (4-7 units - males/3-5 units - females), *harmful drinker* (>8 units-males/>6 units -females).

Smoking at age: 20, 25, 31, 36, 43, 53, 60-64. Information about smoking was collected via interviews and questionnaires. Three categories were derived as follows: *non-smoker* (0 cigarettes daily), *light - moderate smoker* (1-20 cigarettes daily), *heavy smoker* (>20 cigarettes daily).

Pack-years of smoking were calculated by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked across the entire adult period from age 20 to 60-64. Four categories were derived: *non-smoker* (0 pack years), 0.1 –14 *pack years*, 15–39 *pack years* and 40 + *pack years*.

Confounding variables were sex, childhood cognition at age 8 (a summary of 8 cognitive tests), educational attainment by age 26 and social class across midlife (26-43), using the UK Registrar General's Standard's Occupation Classification.

The original size of the study sample was 5,362. The specific number of participants included in these analyses is provided in the tables below.

2.3. Data analysis

Multivariable logistic regression was used to test associations between alcohol and smoking across midlife and low cognitive scores (memory and speed) in early later life (60-64y), adjusting for potential confounders. Data were analyzed using Stata software, Version 12 (StataCorp, 2012).

3. Results

Overall, the sample was equally distributed among sexes. As pointed out by Kuh et al. the response rate of the sample dropped under 80% only once over the 25 waves of data collection. This data can, therefore, be considered a representative sample of the population.

Memory scores were normally distributed across the sample. Overall, 821 participants were assigned to the 'low memory scores' category and 1,157 participants into the 'low-speed scores' category. Those with missing scores on cognition at the age of 60-64 had significantly lower childhood cognition scores at the age of 8 ($p<0.001$) and lower education by the age of 26 ($p<0.001$). Alcohol drinking and smoking patterns were similar for both groups.

The majority of the participants were in low-moderate drinking categories, at all ages investigated. Harmful drinking represented approximately 5% of the sample. There was a slight, but steady increase across the lifespan in heavy drinking. Non-drinkers and harmful drinkers had lower cognition at age 8 ($p<0.001$) than low-moderate and heavy drinkers.

A significant association was also found between alcohol and social class. Most heavy and harmful drinkers were found to be in managerial and technical occupation. The second highest number of harmful drinkers was in the manual social class.

Lastly, there was a significant association between alcohol and education. At ages 36-43, most of the heavy and harmful drinkers had none education attempted. At age 53, most of the heavy and hazardous drinkers obtained at least A-levels education. At the age of 60-64, the pattern was not longer clear; most heavy drinkers gained an A-level education, whereas most harmful drinkers had a vocational education.

Between ages 25 to 31, there were more smokers than non-smokers. From age 36, smoking behavior, in general, started to decrease. Between the ages 53 to 60-64 more than 2/3 of participants were non-smokers.

Childhood cognition was a significant association with smoking across midlife from 36 onwards at all ages ($p<0.001$). Heavy smokers had significantly lower cognition at age 8, compared to moderate smokers and non-smokers.

There was a significant association between smoking and social class. Up to the age of 36 most heavy smokers were in class II, from the age of 43 most heavy smokers were in class III (manual). At all ages, there was a significant association between smoking and education; as the level of education increased, smoking decreased. Heavy smokers across midlife had no formal education.

3.1. Alcohol and cognition

Table 1 shows the results of logistic regression between alcohol consumption and low memory scores.

At age 36 there was a trend towards lower odds of low memory scores at the age of 60-64 for drinking at all levels. This trend, however, did not reach statistical significance. At age 53 there was a significant inverse association between heavy drinking and low memory scores ($p=0.05$). The odds of low memory scores were 0.67 lower for heavy drinkers compared to non-drinkers. Same odds for inverse association were observed at the age of 60-64 ($p=0.02$).

Table 2 shows the results of logistic regression that was also testing the association between alcohol consumption across lifespan and memory scores. At age 36 inverse non-significant patterns were observed again. The association between heavy drinking at age 53 and lower odds of low memory scores remained significant even when adjusted for smoking ($p=0.05$). Similarly, at age 60-64, heavy drinking was significantly associated with 0.70 lower odds of low memory scores.

The current results testing associations between alcohol consumption across midlife and memory in later life showed some associations but no clear patterns. Drinking across midlife appears to be protective against lower memory scores in later life, although at the ages of 36 and 43 these associations were explained by various confounders such as early cognition at age 8, education or adult social class. In contrast, harmful drinking at 43 and 53 years was associated with higher odds of low memory scores in later life; however, these associations were not significant. This might potentially indicate that a possible sensitive period for harmful drinking could start after age 36 and be observed between the ages 43-53, or that this association may be consistently modest across the life course.

Table 3 shows results of logistic regression testing associations between alcohol consumption and low-speed scores. At age 36 there was a trend of higher odds of the low-speed scores for any level of drinking. For harmful drinkers, this association was significant ($p=0.04$). At age 43, a similar pattern was observed, and the association reached significance for both heavy ($p=0.01$) and harmful drinkers ($p=0.03$). At age 53 there was a significant inverse association between low-moderate drinking and low memory scores ($p=0.03$).

Table 4 shows the results for the models presented in Table 3 further adjusted for alcohol consumption. The association between harmful drinking at the age of 36 and higher odds of low-speed scores no longer reached significance when smoking was added to the model ($p=0.07$). At the age of 43, both associations between heavy drinkers and harmful drinkers and higher odds of low-speed scores remained significant ($p=0.01$). The inverse association at the age of 53, also remained significant ($p=0.03$).

Drinking heavily, particularly at the age of 43, was associated with higher odds of low-speed scores in later life independent of several confounders' adjustments and smoking at the same age. In contrast, low-moderate drinking at 53 years was associated with significantly lower odds of low-speed scores in later life. This might

potentially indicate that a possible sensitive period for harmful drinking could start after the age of 36 and its effects are observed at the age of 43. In contrast, sensible drinking (low-moderate) starting from the age 53 onwards could be protective of speeded performance, independent of smoking and other confounders.

3.2. Smoking and cognition

Table 5 shows results of the associations between smoking and memory. Until the age of 36, no significant association was found, but there was a trend of heavy smokers having higher odds of low memory scores. From the age of 36 onwards, the association between heavy smoking and higher odds of low memory scores was significant. The highest odds of memory scores were observed for smoking at the age of 53 (OR=2.17).

Table 6 shows the results for the models presented in Table 5 further adjusted for alcohol. The significant association that was found at the ages 53 and 60-64 was explained when alcohol drinking was added to the model. At the age of 36, the association remained significant (p=0.01) as well as at the age of 43 (p=0.01). Overall at all ages, a trend of heavy smoking having higher odds of low memory scores at the age of 60-64 was observed.

Smoking across midlife, especially from the age of 36 onwards was significantly associated with higher odds of low memory scores at 60-64. However, at the ages 53 and 60-64, these associations were explained by alcohol consumptions at similar ages.

Table 7 shows results of logistic regression testing association between smoking across the lifespan and low-speed scores adjusted for confounders only. The pattern was no longer clear. At the age of 36, smoking more than 20 cigarettes a day was significantly associated with higher odds of the low-speed scores (p=0.002). At the age of 53 there was a significant association between light smoking and lower speed scores, and at the age of 60-64, there was a significant association between heavy smoking and low-speed scores. Overall, there was a trend of smoking being associated with higher odds of low memory scores. The reason for no further significant association may be the lack of power caused by the small sample size of heavy smokers in some age-groups.

Table 8 shows the results for the models presented in Table 7 further adjusted for alcohol. Similarly, to the previous model, there was a trend of heavy smoking being associated with higher odds of low-speed scores. The association at age 36 remained significant, the odds being 2.58 higher for heavy smokers to have lower speed scores compared to non-smokers. Alcohol consumption explained the associations at the ages of 53 and 60-64.

Smoking from age 36 onwards was associated with higher odds of the low-speed scores at 60-64. However, most of these associations were explained by alcohol consumptions at similar ages, except for heavy smoking at age 36, which remained significant (p=0.002).

3.3. Smoking and drinking across lifespan and cognition

Smoking and drinking across lifespan and memory

Table 9 shows results of the association between pack-years and memory adjusted for confounders as well as mean alcohol consumption across the lifespan. There was a significant association between high pack years (40+) and low memory scores, even when adjusting for alcohol.

Table 10 shows a similar model to that of Table 9, but the association was tested for the low-speed scores. Similarly, when adjusting for alcohol, there was a significant association between more than 40 pack years and low-speed scores (p=0.04).

Overall, high pack-years were significantly associated with low memory and speed scores even after adjustment for mean alcohol consumption across the lifespan.

4. Discussion

Data from the 1946 British Birth Cohort was analyzed to test associations between smoking and drinking behaviors across midlife, about cognitive impairment in later life. The study began in 1946 and included information across 25 waves of data collection.

There were significant associations observed between alcohol consumption and cognitive performance on speed tests. The results on alcohol consumption and memory suggest that there are no clear patterns. Overall, there was an indication that potential sensitive periods of harmful drinking might start after the age of 36 and could be observed between the ages 43–53.

Some of these association did not remain significant after adjusting for confounders, and even harmful drinking did not reach statistical significance. Similarly, in a prospective study of 1,309 women aged 65 years and older, the adjustment for age, education, diabetes, smoking, BMI, and physical activity attenuated the magnitude of the effect of decreased alcohol consumption on cognitive impairment and resulted in borderline statistical significance [35]. Overall, there was some evidence for protective effects of moderate alcohol consumption as suggested previously by Antilla et al. [9]. Heavy drinking was significantly associated with higher odds of low-speed scores in later life, and the protective effect of alcohol consumption was observed from the age of 53 onwards. These results extend the previous findings of Richards et al. by highlighting that the stronger decline in letter search speed in women observed over the 10-year period in his investigation in the 1946 British Birth Cohort [36] and echoes the observations made by Espeland, in his study, in which drinking one or more units per day was associated with significant declines in cognitive function in women in comparison to abstention [37]. Our findings on alcohol consumption are also in agreement with those from the Whitehall II study, where excessive alcohol consumption in men (≥36 g/d) was associated with faster cognitive decline compared with light to moderate alcohol consumption [38].

There is a clearer pattern of results on smoking and cognitive impairment. No positive effects of smoking were found throughout the lifespan Smoking was significantly associated with lower memory and speed scores. An increase in the number of smoking pack-years was associated with low memory and slow search speed. The highest risk of cognitive impairment in both speed and memory tests was for those with 40 pack years or more indicating the level of smoking two pack of cigarettes every day for 20 years or one pack of cigarettes per day for 40 years. Similar to drinking patterns, the possible sensitive period for the detrimental effects of smoking on memory impairment might be observed mainly between the ages 36 – 43. The small sample size may explain the fact that occasionally no significant associations were shown, and we might also be facing the issue of "survivor effects". Overall, the current results build on the previous research conducted by Richards et al., which showed that heavy smokers showed a significant cognitive decline over ten years period from 43 to 53 years in the same cohort study. Similar findings of smoking on cognitive change from age 11 to 66 years were found by Starr et al. [25].

4.1. Strengths and limitations

Given the nature of this study, a longitudinal research with multiple waves of data collection allows seeing whether the effects of harmful lifestyle behaviors are long-lived and would remain significant across a longer period. Secondly, using a representative sample of the English population, there is an increased possibility to generalize these findings to the wider population. The amount of data collected led to the opportunity to control for multiple confounders and thus increase the reliability of the results obtained.

The categories of drinking and smoking were derived in this analysis according to the Department of Health guidelines, ensuring cross studies examinations.

There are, however, also certain limitations that need to be considered. Some of the data were collected via self-reported food diaries, and this might potentially mean that it is not an accurate representation of the real alcohol consumption due to the issue of underreporting. The second limitation can be related to the lower number of people observed in older age and thus result in loss of power. Therefore, these results need to be taken with caution as the sample size in later life decreased, possibly due to the low survival effect of heavy smokers.

4.2. Implications

These results might suggest that there are possible sensitive periods for the harmful effects of smoking and drinking that can occur after the age of 36 and were persistently observed between the ages of 43–53. On the other hand, sensible drinking, especially from the age of 53 onwards seems to be protective of speed performance. This might suggest that intervention may be more beneficial in the decades preceding clinical manifestation of neuropathological burden. Our results also indicate that it might be crucial to highlighting the importance of smoking cessation; due to the negative role smoking has on cognitive performance, especially in memory. Further implication lies in the fact that since smoking is associated with dementia, as seen in the growing evidence from multiple studies, those smokers that live to an older age are faced with a high risk of dementia.

5. Conclusion

Overall, this study identified the groups that are at higher risk of cognitive impairment and dementia, such as heavy smokers and heavy alcohol drinkers. The key contribution is the identification of the sensitive period for harmful drinking and smoking associated with higher risk of cognitive impairment. It is important to consider smoking cessation, as a key factor that might prevent faster cognitive impairment.

References

1. Lautenschlager, N., Almeida, O., & Flicker, L. (2003). Preventing Dementia: Why We Should Focus on Health Promotion Now. International Psychogeriatrics, 15, 111 - 119. doi:10.1017/S1041610203008809

2. Ferri, C., Prince, M., Brayne, C., Brodaty, H., Fratiglioni, L., Ganguli, M., Scazufca, M. (2005). Global prevalence of dementia: a Delphi consensus study. Lancet, 366, 2112 - 2117. doi:10.1016/S0140-6736(05)67889-0

3. Fujishima, M., & Kiyohara, Y. (2002). Incidence and risk factors of dementia in a defined elderly Japanese population. Annals New Yokr Academy of Sciences, 977, 1 - 8. doi:10.1111/j.1749-6632.2002.tb04793.x

4. Lindenberger, U. (2014). Human cognitive aging: Corriger la fortune? Science, 346, 572 - 578. doi: 10.1126/science.1254403

5. Cadar, D., Pikhart, H., Mishra, G., Kuh, D., & Richards, M. (2012). The role of lifestyle behaviours on 20-year cognitive decline. Journal of Aging Research, 2012. doi:10.1155/2012/304014

6. van Gelder, B. M., Tijhuis, M. A., Kalmijn, S., Giampaoli, S., Nissinen, A., & Kromhout, D. (2004). Physical activity in relation to cognitive decline in elderly men The FINE study. Neurology, 63, 2316 - 2321. doi:10.1212/01.WNL.0000147474.29994.35

7. Sabia, S., Nabi, H., Kivimaki, M., Shipley, M. J., Marmot, M. G., & Singh-Manoux, A. (2009). Health Behaviors From Early to Late Midlife as Predictors of Cognitive Function. American Journal of Epidemiology, 170, 428 - 437. doi:10.1093/aje/kwp161

8. Pronk, N. P., Anderson, L. H., Crain, L., Martinson, B. C., O'Connor, P. J., Sherwood, N. E., & Whitebird, R. R. (2004). Meeting recommendations for multiple healthy lifestyle factors Prevalence, clustering, and predictors among adolescent, adult, and senior health plan members. American Journal of Preventive Medicine, 27, 25 - 33. doi:10.1016/j.amepre.2004.04.022

9. Antilla, T., Helkala, E.-L., Viitanen, M., Kareholt, I., Fratiglioni, L., Winblad, B., Kivipelto, M. (2004). Alcohol drinking in middle age and subsequent risk of mild cognitive impairment and dementia in old age: a prospective

10. Elias, P. K., Elias, M. F., D'Agostino, R. B., Silbershatz, H., & Wolf, P. A. (1999). Alcohol consumption and cognitive performance in the Framingham Heart Study. American Journal of Epidemiology, 150, 580 - 589.

11. House of Commons: Science and Technology Committee. (2011). Alcohol guidelines. London: The Stationery Office Limited. Retrieved from http://www.publications.parliament.uk/pa/cm201012/cmselect/cmsctech/1536/1536.pdf

12. Park, B., Park, J., Jun, J. K., Choi, K. S., & Suh, M. (2013). Gender differences in the association of smoking and drinking with the development of cognitive impairment. PloS one, 8(10), e75095.

13. Luchsinger, J., Tang, M.-X., Siddiqui, M., Shea, S., & Mayeux, R. (2004). Alcohol intake and risk of dementia. JAGS, 52, 540 - 546. doi:10.1111/j.1532-5415.2004.52159.x

14. Peters, R., Peters, J., Warner, J., Beckett, N., & Bulpitt, C. (2008). Alcohol, dementia and cognitive decline in the elderly: a systematic review. Age and Ageing, 37, 505 - 512. doi:10.1093/ageing/afn095

15. Lyvers, M., & Tobias-Webb, J. (2010). Effects of acute alcohol consumption on executive cognitive functioning in naturalistic settings. Addictive Behaviours, 35, 1021 - 1028. doi: 10.1016/j.addbeh.2010.06.022

16. Parker, D. A., Parker, E. S., Brody, J. A., & Schoenberg, R. (1983). Alcohol use and cognitive loss among employed men and women. American Journal of Public Health, 73, 521 - 527. doi:10.2105/AJPH.73.5.521

17. Parker, E. S., Parker, D. A., Brody, J. A., & Schoenberg, R. (1982). Cognitive Patterns Resembling premature aging in male social drinkers. Alcoholism: Clinical and experimental research, 6, 46 - 53. doi:10.1111/j.1530-0277.1982.tb05380.x

18. Thomas, V., & Rockwood, K. (2001). Alcohol Abuse, Cognitive Impairment, and Mortality Among Older People. Journal of the American Geriatrics Society, 49, 415 - 420. doi:10.1046/j.1532-5415.2001.49085.x

19. Cadar, D., Pikhart, H., Mishra, G., & Richards, M. (2011). The long and short term effects of alcohol consumption on cognitive decline. Journal of Epidemiology and Community Health, 65(Suppl 2), A33-A34.

20. Reitz, C., den Heijer, T., & van Duijn, C. (2007). Relation between smoking and risk of dementia and Alzheimer disease: The Rotterdam Study. Neurology, 69, 998 - 1005. doi:10.1212/01.wnl.0000271395.29695.9a

21. Brody, A. L., Mandelkern, M. A., Jarvik, M. E., Lee, G. S., Smith, E. C., Huang, J. C., Lodnon, E. D. (2004). Differences between smokers and nonsmokers in regional gray matter volumes and densities. Biology PSychiatry, 55, 77 - 84. doi:10.1016/S0006-3223(03)00610-3

22. Hanlon, C. A., Owens, M. M., Joseph, J. E., Zhu, X., George, M. S., Brady, K. T., & Hartwell, K. J. (2014). Lower subcortical gray matter volume in both younger smokers and established smokers relative to non-smokers. Addiction Biology. doi:10.1111/adb.12171

23. Fritz, H.-C., Wittfeld, K., Schmidt, C. O., Domin, M., Grabe, H. J., Hegenscheid, K., Lotze, M. (2014). Current smoking and reduced gray matter volume-a voxel-based morphometry study. Neuropsychopharmacology, 39, 2594 - 2600. doi:10.1038/npp.2014.112

24. Tyas, S., White, L., Petrovitch, H., Ross, W., Foley, D., Heimovitz, H., & Launer, L. (2003). Mid-life smoking and late-life dementia: The Honolulu-Asia Aging Study. Neurobiology of aging, 24, 589 - 596. doi:10.1016/S0197-4580(02)00156-2

25. Starr, J., Deary, I., Fox, H., & Whalley, L. (2007). Smoking and cognitive change from age 11 to 66 years: A confirmatory investigation. Addictive Behaviours, 32, 63 - 68. doi:10.1016/j.addbeh.2006.03.020

26. Richards, M., Jarvis, M. J., Thompson, N., & Wadsworth, M. E. (2003). Cigarette Smoking and Cognitive Decline in Midlife evidence from a prospective birth cohort study. American Journal of Public Health, 93, 994 - 999. doi:10.2105/AJPH.93.6.994

27. Anstey, K., von Sanden, C., Salim, A., & O' Kearney, R. (2007). Smoking as a Risk Factor for Dementia and Cognitive Decline: A Meta-Analysis of Prospective Studies. American Journal of Epidemiology, 166, 367 - 378. doi:10.1093/aje/kwm116

28. Lee, Y., Hwan Back, J., Kim, J., Kim, S.-H., Na, D. L., Cheong, H.-K., Kim, Y. G. (2010). Systematic Review of Health Behavioural Risks and Cognitive Health in Older Adults. International Psychogeriatrics, 22, 174 - 187. doi:10.1016/j.ypmed.2008.10.021

29. Lindsay, J., Laurin, D., Verreault, R., Hebert, R., Helliwell, B., Hill, G., & McDowell, I. (2002). Risk factors for Alzheimer's disease a prospective analysis from the Canadian Study of Health and Aging. American Journal of Epidemiology, 156, 445 - 454. doi:10.1093/aje/kwf074

30. Patterson, C., Feightner, J., Garcia, A., & MacKnight, C. (2007). General risk factors for dementia: a systematic evidence review. Alzheimer's & Dementia, 3, 341 - 347. doi:10.1016/j.jalz.2007.07.001

31. Bell, C.L., Chen, R., Masaki, K., Yee, P., He, Q., Grove, J., Donlon, T., Curb, J.D., Willcox, D.C., Poon, L.W. and Willcox, B.J. (2014). Late-life factors associated with healthy aging in older men. Journal of the American Geriatrics Society, 62(5), pp.880-888.population-based study. BMJ Open. doi:10.1136/bmj.38181.48958.BE

32. Zhou, H., Deng, J., Li, J., Wang, Y., Zhang, M., & He, H. (2003). Study of the relationship between cigarette smoking, alcohol drinking and cognitive impairment among elderly people in China. Age and ageing, 32(2), 205-210.

33. Richards, M., & Hatch, S. L. (2011). A life course approach to the development of mental skills. The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, gbr013.

34. Kuh, D., Pierce, M., Adams, J., Deanfield, J., Ekelund, U., Frilberg, P., Hardy, R. (2011). Cohort profile: updating the cohort profile for the MRC National Survey of Health and Development: a new clinic-based data collection for ageing research. International Journal of Epidemiology, 40, e1 - e9. doi:10.1093/ije/dyq231

35. Hoang, T.D., Byers, A.L., Barnes, D.E., Yaffe, K. (2014). Alcohol consumption patterns and cognitive impairment in older women. Am J Geriatr Psychiatry. doi:10.1016/j.jagp.2014.04.006

36. Richards, M., Hardy, R., & Wadsworth, M. E. J. (2005). Alcohol consumption and midlife cognitive change in the British 1946 birth cohort study. Alcohol and Alcoholism, 40, 112-117.

37. Espeland, M. A., Gu, L., Masaki, K. H., Langer, R. D., Coker, L. H., Stefanick, M. L. et al. (2005). Association between reported alcohol intake and cognition: Results from the Women's Health Initiative Memory Study. American Journal of Epidemiology, 161, 228-238.

38. Sabia, S., Elbaz, A., Britton, A., Steven, B., Dugravot, A., Shipley, M. J., Kivimaki, M., & Singh-Manoux, A. (2014). Alcohol consumption and cognitive decline in early old age. Neurology, 82(4): 332–339. doi: 10.1212/WNL.0000000000000063

TABLES

TABLE 1 - Odds Ratio for alcohol drinking at each age on low memory at the ages of 60 - 64

	OR (95% CI)	*P*	N
Alcohol consumption at 36 (reference - non-drinker)			313
low-moderate	0.86 (0.63, 1.16)	.33	759
heavy	0.72 (0.48, 1.07)	.11	251
harmful	0.79 (0.41, 1.53)	.49	57
		N = 1380	
Alcohol consumption at 43 (reference - non-drinker)			435
low-moderate	0.78 (0.60, 1.01)	.06	891
heavy	0.87 (0.62, 1.21)	.40	325
harmful	1.36 (0.79, 2.33)	.26	84
		N = 1735	
Alcohol consumption at 53 (reference - non-drinker)			261
low-moderate	0.77 (0.55, 1.08)	.14	577
heavy	0.67 (0.44, 1.00)	.05	283
harmful	1.26 (0.65, 2.43)	.50	57
		N = 1178	
Alcohol consumption at 60 - 64 (reference - non-drinker)			425
low-moderate	0.82 (0.62, 1.09)	.18	669
heavy	0.67 (0.48, 0.94)	.02	375
harmful	0.77 (0.44, 1.34)	.36	86
		N = 1555	

Note. All odds ratios were adjusted for sex, cognitive score at age 8, education and SES. CI = Confidence Interval, N = number of people in each category

TABLE 2 - Odds Ratio for alcohol drinking at each age on low memory at   age 60 -
64

	OR (95% CI)	*P*	N
Alcohol consumption at 36 (reference - non-drinker)			313
low-moderate	0.86 (0.64, 1.17)	.34	757
heavy	0.70 (0.47, 1.04)	.08	249
harmful	0.70 (0.35, 1.39)	.31	54
			N = 1373
Alcohol consumption at 43 (reference - non-drinker)			435
low-moderate	0.78 (0.60, 1.02)	.07	891
heavy	0.85 (0.60, 1.19)	.34	325
harmful	1.23 (0.71, 2.13)	.46	84
			N = 1735
Alcohol consumption at 53 (reference - non-drinker)			261
low-moderate	0.78 (0.56, 1.09)	.15	577
heavy	0.67 (0.44, 1.00)	.05	282
harmful	1.18 (0.60, 2.30)	.63	57
			N = 1177
Alcohol consumption at 60 - 64 (reference - non-drinker)			387
low-moderate	0.86 (0.64, 1.15)	.31	629
heavy	0.70 (0.49, 1.00)	.05	350
harmful	0.81 (0.46, 1.44)	.47	80
			N = 1446

Note. All ratios were adjusted for sex, cognitive score at age 8, education, SES and smoking. CI = Confidence Interval, N = number of people in each category

TABLE 3 - Odds Ratio for alcohol drinking at each age on low speed at age 60 - 64

	OR (95% CI)	*P*	N
Alcohol consumption at 36 (reference - non-drinker)			321
low-moderate	1.06 (0.81, 1.40)	.66	767
heavy	1.17 (0.82, 1.66)	.38	253
harmful	1.91 (1.02, 3.57)	.04	57
			N = 1398
Alcohol consumption at 43 (reference - non-drinker)			442
low-moderate	1.21 (0.96, 1.53)	.11	906
heavy	1.49 (1.10, 2.01)	.01	325
harmful	1.76 (1.06, 2.91)	.03	85
			N = 1758
Alcohol consumption at 53 (reference - non-drinker)			265
low-moderate	0.71 (0.52, 0.96)	.03	584
heavy	1.06 (0.74, 1.51)	.74	287
harmful	1.73 (0.92, 3.25)	.09	57
			N = 1193
Alcohol consumption at 60 -64 (reference - non-drinker)			429
low-moderate	0.93 (0.72, 1.20)	.59	673
heavy	1.18 (0.88, 1.58)	.28	379
harmful	1.16 (0.71, 1.89)	.55	84
			N = 1565

Note. All ratios were adjusted for sex, cognitive score at age 8, education and SES. CI = Confidence Interval, N = number of people in each category

TABLE 4 - Odds Ratio for alcohol drinking at each age on low speed at age 60 - 64

	OR (95% CI)	*P*	N
Alcohol consumption at 36 (reference - non-drinker)			321
low-moderate	1.07 (0.81, 1.41)	.64	765
heavy	1.14 (0.80, 1.62)	.48	251
harmful	1.83 (0.95, 3.52)	.07	54
			N = 1391
Alcohol consumption at 43 (reference - non-drinker)			442
low-moderate	1.22 (0.96, 1.54)	.10	906
heavy	1.47 (1.08, 1.98)	.01	325
harmful	1.67 (1.01, 2.78)	.05	85
			N = 1758
Alcohol consumption at 53 (reference - non-drinker)			265
low-moderate	0.71 (0.52, 0.96)	.03	584
heavy	1.06 (0.75, 1.52)	.73	286
harmful	1.71 (0.90, 3.23)	.10	57
			N = 1192
Alcohol consumption at 60 -64 (reference - non-drinker)			391
low-moderate	0.94 (0.72, 1.22)	.63	632
heavy	1.23 (0.91, 1.67)	.18	354
harmful	1.16 (0.70, 1.94)	.56	78
			N = 1455

Note. All ratios were adjusted for sex, cognitive score at age 8, education, SES and smoking. CI = Confidence Interval, N = number of people in each category

TABLE 5 - Odds Ratio for smoking at each age on low memory at age
60 - 64

	OR (95% CI)	*P*	N
Smoking at age 20 (reference: non-smoker)			864
1-20 cigarettes	1.06 (0.84, 1.34)	.61	745
>20	2.00 (0.84, 4.72)	.12	29
			N = 1638
Smoking at age 25 (reference: non-smoker)			826
1-20 cigarettes	1.00 (0.79, 1.27)	.98	690
>20	1.25 (0.69, 2.29)	.46	57
			N = 1573
Smoking at age 31 (reference: non-smoker)			779
1-20 cigarettes	0.87 (0.68, 1.11)	.25	661
>20	1.33 (0.93, 1.90)	.12	207
			N = 1647
Smoking at age 36 (reference: non-smoker)			1242
1-20 cigarettes	1.11 (0.84, 1.45)	.46	355
>20	1.88 (1.18, 3.00)	0,008	102
			N = 1699
Smoking at age 43 (reference: non-smoker)			1356
1-20 cigarettes	1.20 (0.90, 1.59)	.22	304
>20	2.03 (1.26, 3.27)	0,004	97
			N = 1757
Smoking at age 53 (reference: non-smoker)			1428
1-20 cigarettes	1.35 (1.00, 1.81)	.05	264
>20	2.17 (1.19, 3.96)	.01	58
			N = 1750
Smoking at age 60 - 64 (reference: non-smoker)			1481
1-20 cigarettes	1.38 (0.88, 2.16)	.16	102
>20	1.73 (1.05, 2.86)	.03	84
			N = 1667

Note. All ratios were adjusted for sex, cognitive score at age 8, education
and SES. CI = Confidence Interval, N = number of people in each
category

TABLE 6 - Odds Ratio for smoking at each age on low memory at age 60 - 64

	OR (95% CI)	*P*	N
Smoking at age of 20 (reference: non-smoker)			864
1-20 cigarettes	1.06 (0.84, 1.34)	.61	745
>20	2.00 (0.84, 4.72)	.12	29
			N = 1638
Smoking at age of 25 (reference: non-smoker)			826
1-20 cigarettes	1.00 (0.79, 1.27)	.98	690
>20	1.25 (0.69, 2.29)	.46	57
			N = 1573
Smoking at age of 31 (reference: non-smoker)			779
1-20 cigarettes	0.87 (0.68, 1.11)	.25	661
>20	1.33 (0.93, 1.90)	.12	207
			N = 1647
Smoking at age of 36* (reference: non-smoker)			1029
1-20 cigarettes	1.11 (0.82, 1.52)	.50	276
>20	2.05 (1.15, 3.66)	.02	68
			N = 1373
Smoking at age of 43* (reference: non-smoker)			1339
1-20 cigarettes	1.19 (0.89, 1.58)	.24	301
>20	1.84 (1.13, 3.00)	.01	95
			N = 1735
Smoking at age of 53 * (reference: non-smoker)			989
1-20 cigarettes	1.13 (0.76, 1.67)	.55	162
>20	2.10 (0.84, 5.26)	.11	26
			N = 1177
Smoking at age of 60 - 64 * (reference: non-smoker)			1298
1-20 cigarettes	1.54 (0.94, 2.53)	.09	84
>20	1.55 (0.87, 2.73)	.13	64
			N = 1446

Note. All ratios were adjusted for sex, cognitive score at age 8, education, SES and alcohol drinking*. CI = Confidence Interval, N = number of people in each category

TABLE 7 - Odds Ratio for smoking at each age on low speed at age 60 - 64

	OR (95% CI)	*P*	N
Smoking at age 20 (reference: non-smoker)			874
1-20 cigarettes	1.06 (0.86, 1.29)	.60	757
>20	1.85 (0.80, 4.29)	.15	30
			N = 1661
Smoking at age 25 (reference: non-smoker)			832
1-20 cigarettes	1.02 (0.83, 1.25)	.88	702
>20	1.58 (0.88, 2.81)	.12	57
			N = 1591
Smoking at age 31 (reference: non-smoker)			784
1-20 cigarettes	1.03 (0.83, 1.27)	.80	673
>20	1.15 (0.83, 1.60)	.39	209
			N = 1666
Smoking at age 36 (reference: non-smoker)			1250
1-20 cigarettes	1.05 (0.82, 1.33)	.71	368
>20	2.10 (1.32, 3.35)	0,002	101
			N = 1719
Smoking at age43 (reference: non-smoker)			1370
1-20 cigarettes	1.26 (0.98, 1.64)	.08	314
>20	1.30 (0.83, 2.02)	.25	95
			N = 1779
Smoking at age 53 (reference: non-smoker)			1442
1-20 cigarettes	1.37 (1.04, 1.80)	.02	270
>20	1.49 (0.84, 2.63)	.17	58
			N = 1770
Smoking at age 60 - 64 (reference: non-smoker)			1497
1-20 cigarettes	0.89 (0.59, 1.34)	.57	105
>20	1.79 (1.09, 2.95)	.02	82
			N = 1684

Note. All ratios were adjusted for sex, cognitive score at age 8, education and SES.
CI = Confidence Interval, N = number of people in each category

TABLE 8 - Odds Ratio for smoking at each age on low speed at age 60 - 64

	OR (95% CI)	*P*	N
Smoking at age 20 (reference: non-smoker)			874
1-20 cigarettes	1.06 (0.86, 1.29)	.60	757
>20	1.85 (0.80, 4.29)	.15	30
			N = 1661
Smoking at age 25 (reference: non-smoker)			832
1-20 cigarettes	1.02 (0.83, 1.25)	.88	702
>20	1.58 (0.88, 2.81)	.12	57
			N = 1591
Smoking at age 31 (reference: non-smoker)			784
1-20 cigarettes	1.03 (0.83, 1.27)	.80	673
>20	1.15 (0.83, 1.60)	.39	209
			N = 1666
Smoking at age 36 * (reference: non-smoker)			1037
1-20 cigarettes	0.94 (0.71, 1.24)	.66	288
>20	2.58 (1.40, 4.74)	0,002	66
			N = 1391
Smoking at age 43* (reference: non-smoker)			1354
1-20 cigarettes	1.21 (0.93, 1.57)	.16	311
>20	1.25 (0.79, 1.96)	.34	93
			N = 1758
Smoking at age 53* (reference: non-smoker)			1001
1-20 cigarettes	1.07 (0.75, 1.52)	.70	165
>20	1.01 (0.44, 2.32)	.98	26
			N = 1192
Smoking at age 60 - 64* (reference: non-smoker)			1307
1-20 cigarettes	0.93 (0.59, 1.46)	.75	86
>20	1.57 (0.90, 2.75)	.11	62
			N = 1455

Note. All ratios were adjusted for sex, cognitive score at age 8, education, SES and alcohol drinking*. CI = Confidence Interval, N = number of people in each category

TABLE 9 - Odds Ratio for pack years smoking at each age on low memory at age 60 - 64

	OR (95% CI)	*P*	N
Pack years (reference: non-smoker)			542
0.1 - 14 pack years	0.86 (0.65, 1.14)	.29	562
15 - 39 pack years	1.09 (0.78, 1.52)	.61	288
40 + pack years	2.06 (1.28, 3.31)	0,003	112
			N = 1504
Pack years * (reference: non-smoker)			543
0.1 - 14 pack years	0.89 (0.67, 1.18)	.42	560
15 - 39 pack years	1.12 (0.79, 1.57)	.53	285
40 + pack years	2.17 (1.33, 3.54)	0,002	108
			N = 1496

Note. All odds ratios were adjusted for sex, cognitive score at age 8, education, SES and alcohol mean across lifespan*. CI = Confidence Interval, N = number of people in each category

TABLE 10 - Odds Ratio for pack years smoking at each age on low
speed at age 60 - 64

	OR (95% CI)	*P*	N
Pack years (reference: non-smoker)			543
0.1 - 14 pack years	1.02 (0.80, 1.30)	.85	570
15 - 39 pack years	1.24 (0.92, 1.67)	.16	298
40 + pack years	1.80 (1.14, 2.84)	.01	111
			N = 1522
Pack years * (reference: non-smoker)			538
0.1 - 14 pack years	0.97 (0.76, 1.24)	.81	568
15 - 39 pack years	1.13 (0.83, 1.53)	.44	295
40 + pack years	1.65 (1.03, 2.64)	.04	110
			N = 1511

Note. All odds ratios were adjusted for sex, cognitive score at age 8, education, SES, and alcohol mean across lifespan*. CI = Confidence Interval, N = number of people in each category