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Authors

Paganini-Hill, Annlia

Kawas, Claudia H

Corrada, Maria M

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Lifestyle factors and dementia in the oldest-old: The 90+ Study

Annlia Paganini-Hill, PhD[1], **Claudia H Kawas, MD**[1,2,3], and **Maria M Corrada, DrSc**[1,2]

[1]Department of Neurology, University of California at Irvine, Irvine, California

[2]Institute for Memory Impairment and Neurological Disorders, University of California at Irvine, Irvine, California

[3]Department of Neurobiology and Behavior, University of California at Irvine, Irvine, California

Abstract

Dementia incidence increases exponentially with age even in people aged 90 years and older. Because therapeutic regimens are limited, modification of lifestyle behaviors may offer the best means for disease control. To test the hypotheses that lifestyle factors are related to lower risk of dementia in the oldest-old, we analyzed data from The 90+ Study, a population-based longitudinal cohort study initiated in 2003. This analysis included 587 participants (mean age = 93 years) seen in-person and determined not to have dementia at enrollment. Information on lifestyle factors (smoking, alcohol consumption, caffeine intake, vitamin supplement use, exercise and other activities) was obtained at enrollment and was available from data collected 20 years previously. After an average follow-up of 36 months, 268 participants were identified with incident dementia. No variable measured 20 years previously was associated with risk. Engagement in specific activities at time of enrollment, especially going to church/ synagogue and reading, was associated with significantly reduced risk. Consumers of 200+ mg/day of caffeine had a 34 per cent lower risk (HR=0.66, p<0.05) compared with those consuming <50 mg/day. Users of antioxidant vitamin supplements had 25 per cent lower risks compared with non-users. With reading, going to church, caffeine, and vitamin C supplements analyzed together, the HRs changed little and remained significant for reading (0.54, p=0.01) and going to church (HR=0.66, p<0.05) but were not significant for caffeine (HR=0.61, p=0.15) and vitamin C (HR= 0.68, p=0.07). This analysis suggests that lifestyle behaviors at approximately age 70 do not modify risk of late-life dementia. However, participation in activities and caffeine and supplemental vitamin intake around age 90 may reduce risk of dementia in the oldest-old, although cause and effect cannot be determined.

Introduction

Dementia incidence increases exponentially with age doubling approximately every 5 years after age 65 even in people aged 90 years and older.[1,2] Projections of the number of people with dementia from these incidence rates foretell the growing public health burden of dementia in an increasingly aging population.

Corresponding Author: Annlia Paganini-Hill, Clinic for Aging Research & Education, 24361 El Toro Road #150, Laguna Woods, CA 92637, Phone: 949-768-3635, Fax: 949-768-7695, apaganin@uci.edu.

Because therapeutic regimens are limited, modification of lifestyle behaviors may offer the only means for disease control. Several lifestyle behaviors (smoking, alcohol consumption, vitamin intake, physical and other activities) have been found to be associated with future development of dementia in older adults,[3,4] but whether or not lifestyle factors are related to dementia incidence after age 90 – the oldest-old – is not known. Therefore we examined the association of several lifestyle practices on incident dementia in a longitudinal study of the oldest-old.

Methods

Study Population

Participants were part of The 90+ Study, a population-based longitudinal study of aging and dementia among people aged 90 years and older.[2,5] These subjects were originally members of the Leisure World Cohort Study, an epidemiological health study established in the early 1980s of a California retirement community, Leisure World Laguna Hills.[6,7] Individuals alive and aged 90 years and older on January 1, 2003 (n=1144); on January 1, 2008 (n=443); and on or after January 1, 2009 (n=335) were invited to participate. Of the 1919 eligible cohort members, 1581 joined The 90+ Study. We restricted our analysis to the 587 participants who did not have dementia at baseline, as ascertained by an in-person evaluation, and who had at least one additional follow-up evaluation (Figure 1).

Assessments

Participants were asked to undergo an in-person evaluation including a neurological examination (with mental status testing and assessment of functional abilities) by a trained physician or nurse practitioner and a neuropsychological test battery[8] that included the Mini-Mental State Examination (MMSE).[9] For participants whose poor health, frailty, disability, or unwillingness did not allow a full in-person evaluation, information was obtained by telephone or with informants. Participants evaluated by telephone completed the short version of the Cognitive Abilities Screening Instrument (CASI-short).[10] For participants evaluated through informants, the Dementia Questionnaire (DQ)[11–13] was completed over the telephone. All participants (or their informants) completed a questionnaire that included demographics, past medical history, and medication use. In addition, informants of all participants were asked about the participant's cognitive status[14] and functional abilities[15,16] using a mailed questionnaire. Evaluations were repeated every 6 months for in-person participants and annually for participants evaluated by telephone and through informants. The DQ was also completed for all participants shortly after death.

Determination of Cognitive Status

For all participants included in these analyses cognitive status at baseline was determined from an in-person evaluation. Cognitive status at follow-up was also determined from an in-person evaluation for most participants (70%). However, when an in-person evaluation at follow-up was not possible, we used any available information in the following hierarchical order: (1) neurological exam, (2) MMSE, (3) informant questionnaires, and (4) CASI-short. The neurological examiner determined cognitive status applying Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) criteria for dementia[17]. For the MMSE,

we used age- and education-specific cutoff scores for dementia derived from this cohort.[18] For the CASI-short, we used a score 25 as the cutoff score for dementia.[10] Details about the application of the algorithms and the validity of these methods are published elsewhere.[2,5]

Lifestyle Behaviors

Questions on lifestyle behaviors were asked twice: on the original Leisure World Cohort health survey (1981-1985) and repeated at the baseline visit of The 90+ Study (2003-2014).

Smoking

Participants were asked "Have you ever smoked cigarettes during any period of your life (aside from possibly trying them once or twice)?", the greatest number of cigarettes regularly smoked (¼ pack per day, ½ pack per day, 1 pack per day, 1½ packs per day, 2 packs per day or more), age started smoking regularly, and age stopped smoking.

Alcohol Consumption

Consumption of alcoholic beverages was asked separately for wine (4 oz.), beer (12 oz.), and hard liquor (1 oz.), each equivalent to about ½ oz. of alcohol. Response choices for average weekday consumption were: never drink, <1, 1, 2, 3, and 4 or more. Total alcohol intake per day was calculated by summing the number of drinks consumed of each type.

Caffeine Intake

Participants were asked "How many cups or glasses per DAY do you drink of the following — milk, decaffeinated coffee, coffee, black or green tea?" and "How many cans or glasses per WEEK do you drink of the following —cola beverages with sugar, other soft drinks with sugar, cola beverages artificially sweetened, other soft drinks artificially sweetened?" Response choices were none, <1, 1, 2–3, 4–5, and 6+. Also asked was intake of "CHOCOLATE (milk chocolate, fudge, M&M's, Tootsie Rolls, chocolate covered centers, chocolate topping, chocolate cake, chocolate pie, hot chocolate, chocolate milk)". Response choices were rarely or never, a few times per year, about monthly, a few times a month, a few times per week, daily or almost daily. The 90+ Study asked separately about decaffeinated tea and regular tea and decaffeinated and caffeinated soft drinks. We estimated daily caffeine intake by summing the frequency of consumption of each beverage and chocolate multiplied by its average caffeine content (milligrams/standard unit) as 115 for regular coffee, 3 for decaffeinated coffee, 50 for regular tea, 3 for decaffeinated tea, 50 for cola or caffeinated soft drinks, and 6 for chocolate.[19]

Vitamin Supplements

The Leisure World Cohort survey included questions on current use of vitamin supplements in general and specific intake including dose of vitamins A, C and E (multivitamins and individual vitamins). The 90+ Study asked vitamin supplement intake as well, with dose identified from the individual vitamin containers when possible.

Exercise and Other Activities

The amount of time spent on physical activities was ascertained by asking, "On the average weekday, how much time do you spend in the following activities? —Active outdoor activities (e.g., swimming, biking, jogging, tennis, vigorous walking) —Active indoor activities (e.g., exercising, dancing) —Other outdoor activities (e.g., sightseeing, boating, fishing, golf, gardening, attending sporting events) —Other indoor activities (e.g., reading, sewing, crafts, board games, pool, attending theater or concerts, performing household chores) —Watching TV." For each question, the response categories were 0, 15, 30 minutes, 1, 2, 3–4, 5–6, 7–8, 9 hours or more per day. The time spent per day in active activities was calculated by summing the times spent in active outdoor and active indoor activities; in other less physically demanding activities by summing the times spent in other outdoor and other indoor activities.

Additional exercise questions were asked on follow-up questionnaires sent to Leisure World Cohort members in 1983, 1985 and 1998. These asked hours/day spent in vigorous exercise in 1983 and 1998 and whether the participant engaged in moderate or vigorous exercise at age 40.

The 90+ Study also asked participants the time spent (daily or almost daily, a few times per week, a few times per month, about monthly, a few times per year, rarely or never) in the following 16 activities: being outside, going on walks, enjoying nature; being with animals; getting together with family and friends; talking to family and friends on the telephone; going to movies, museums, entertainment; going to church, synagogue, religious events; going shopping for groceries, clothes, etc.; going for a ride in the car; reading or having stories read to you; listening to radio, watching TV; doing vigorous exercise; playing games or cards, doing crosswords, puzzles; doing handiwork or crafts; gardening, indoor or outdoor; traveling with at least one overnight stay; sitting and thinking.

Statistical Analyses

Hazard ratios (HRs) of dementia associated with lifestyle factors as measured by the Leisure World Cohort Study and by The 90+ Study were estimated using Cox regression analysis.[20] Age at study entry was the age at enrollment in The 90+ Study (delayed entry) and the event of interest was age at dementia diagnosis. Given our model used delayed entry (analogous to specifying time-dependent variables), the Cox regression is no longer a proportional hazard model. HRs for each lifestyle variable were adjusted for age using age (continuous) as the fundamental time scale and for sex and education (high school, vocational school or some college, college graduate) by including them as covariates in the model. Participants were followed until age of dementia diagnosis, death or last visit, whichever came first. Statistical analyses were performed using SAS® version 9.3 (SAS Institute Inc., Cary, NC). Separate analyses were done for each lifestyle factor and no adjustment in the p-values was made for multiple comparisons.

Results

At baseline, the participants' ages ranged from 90 to 103 years (mean ± standard deviation = 93 ± 2.6). By the end of followup, which averaged 36 months, 268 participants had been diagnosed with dementia at ages 90 to 106 (mean ± standard deviation = 96 ± 3.0).

Table 1 shows the age-, sex- and education-adjusted HRs of incident dementia for lifestyle factors collected at enrollment in The 90+ Study (in 2003 or later) and by the Leisure World Cohort Study about 20 years previously (in the early 1980s). Few lifestyle factors either at baseline or 20 years previously were associated with risk of incident dementia. Neither smoking, alcohol consumption, caffeine intake or antioxidant vitamin supplement use as reported in the 1980s was related to risk. Neither was active or other exercise in the 1980s nor vigorous exercise in 1983, in 1998, or at age 40. Those reporting intake of 200+ mg/day of caffeine at enrollment in The 90+ Study had a significantly lower risk of dementia (HR=0.66, 95% CI 0.43-0.99) compared with those with intake of <50 mg/day. Users of vitamin A, C or E supplements had significantly lower risks (about 25 per cent) compared with non-users. When all The 90+ Study variables in Table 1 were included in the regression model, the HRs for caffeine were reduced to 0.67 (95% CI 0.41-1.08) for 50-199 mg/day and 0.60 (95% CI 0.33-1.09) for 200+ mg/day. The HR for vitamin C supplement users was reduced to 0.53 (95% CI 0.22-1.26).

Table 2 shows the HRs for specific activities reported at enrollment in The 90+ Study. Six of the 16 activities showed significantly reduced risk in participants. These HRs were 0.53 for shopping for groceries, clothes, etc.; 0.63 for going to movies, museums, entertainment; 0.66 for doing handiworks or crafts; 0.67 for being with animals; 0.71 for going for a ride in the car; and 0.74 for reading or having stories read. In a multivariate analysis including all the activity variables in Table 2, no activity showed a statistically reduced risk of dementia but reading and going to church/synagogue had HRs of 0.68 (p=0.09) and 0.66 (p=0.11).

When caffeine consumption, supplemental vitamin C intake, going to church/synagogue, and reading were considered jointly in a multivariate model, the HRs changed little: 0.61 for high caffeine intake (p=0.15), 0.68 for vitamin C use (p=0.07), 0.66 for going to church/synagogue (p<0.05), and 0.54 for reading (p=0.01).

Discussion

Our longitudinal study in the oldest-old found that few lifestyle factors, either at baseline or 20 years previously, were associated with risk of incident dementia. Only caffeine consumption, supplemental vitamin C intake and selected leisure activities reported at enrollment in The 90+ Study were related to reduced risk.

Leisure activities including those with mental, social and physical components have been related with reduced risk of dementia[21-24] although recent reports have concluded the evidence is insufficient.[25] Our study suggests that continued mental/social activity into the tenth decade of life is associated with a lower risk. However, we found no effect of active or other less physically demanding physical exercise. A recent review identified seven prospective studies of individuals aged 65+ years which evaluated the association between

physical activity and dementia.[26] Although all found some association of physical activity with reduced risk of dementia, no study included the very old.[27-33] In our study specific activities associated with lower risk were shopping for groceries, clothes, etc.; doing handiworks or crafts; reading or having stories read; being with animals; going to movies, museums, entertainment; and going for a ride in the car. In joint analysis reading and going to church/synagogue were the most significant. These activities have a strong mental component. However, reduced activity level at time of enrollment in The 90+ Study may reflect less participation by individuals showing early cognitive deficits and not a real risk reduction.

Our study, which found that consumers of 200+ mg/day of caffeine had a 40% reduced risk of incident dementia, supports previous findings of decreased risk among caffeine or coffee consumers.[34,35] In the prospective CSHA (Canadian Study of Health and Aging) of healthy older (>65 years) adults, regular daily coffee drinking was associated with a 30% lower risk of developing Alzheimer's Disease (AD) over five years.[36] The CAIDE (Cardiovascular Risk Factors, Aging and Dementia) study found that moderate coffee drinkers (3-5 cups/day) at midlife had a 65 per cent lower risk of dementia later in life compared with those drinking no or only little coffee.[37] A small case-control study of 54 older adults with probable AD and age-matched healthy controls reported a strong inverse correlation of caffeine intake and AD risk; intake of 200 mg/day lowered risk by 60% vs. 70 mg/day.[38] Finally, recent prospective data indicated that high plasma caffeine levels were associated with a reduced risk of dementia or a delayed onset in patients with mild cognitive impairment.[39] Although the Honolulu–Asian Aging Study did not find a significant association between caffeine intake and dementia risk, autopsy patients in the highest quartile of caffeine intake (>277.5 mg/day) were less likely to have neuropathological lesions, such as AD-related lesions, microvascular ischemic lesions, cortical Lewy bodies, hippocampal sclerosis, or generalized atrophy.[40] Caffeine is a central nervous system stimulant, has antioxidant properties, may prevent neuronal cell death caused by exposure to β-amyloid, and has shown neuroprotective effects after administration in experimental models of the cerebral nervous hypoxia and ischemia, suggesting plausible biological mechanisms.[34,35] Although caffeine is the most widely consumed behaviorally active substance in the western world and despite epidemiological data on the effects of caffeine in aged subjects and data from animal studies, no clinical trial has examined the extent by which caffeine can reduce disease incidence or slow down progression.

Longitudinal studies have identified significantly increased risks of dementia among tobacco smokers[41,42] and, though less consistently, decreased risks among moderate drinkers of alcohol.[43] These were not associated with dementia risk in our study. Our study population included very few current smokers; only 5 participants were current smokers when they enrolled in The 90+ Study and only 36 in the early 1980s so we could not examine risk in only current smokers. No elevated risk was observed in ever smokers.

Some prospective studies have reported that intake of anti-oxidants are associated with reduced risk of dementia. People with higher intakes of vitamin E and C, either through diet or supplements, have been found to have slower cognitive decline and a lower risk of AD in old age [reviewed in reference 44]. However, other large, prospective observational studies

found no association between vitamin intake and dementia risk. Likewise, evidence from randomized controlled clinical trials is at best inconsistent, with most studies finding no relationship between vitamin E supplementation and cognitive performance.[44,45] In our study of the oldest-old we found supplemental intake of vitamins A, C or E. taken at enrollment in the 90+ Study, but not in the 1980s, was associated with lower dementia risk. As previously reported, more than 90% of the Leisure World Cohort members received the 1980 recommended dietary allowance of the National Research Council for vitamin A (5000 IU for males; 4000 IU for females) from food sources alone.[46] Therefore non-users of supplements were unlikely to have low levels of these antioxidants. We cannot rule out the possibility that long-term antioxidant supplementation may reduce the risk of incident dementia in other populations with lower levels of vitamin intake.

Our study has several limitations and strengths that warrant discussion. Our subjects are from a select population — moderately affluent, highly educated, health conscious, and primarily Caucasian. Although this may limit the generalizability of our results, it reduces potential confounding by race, education, SES, and access to health care. The independent variables used in these analyses are crude and self-reported and their reliability and validity were not ascertained. Although changes over time in potential risk factors may affect outcome, lifestyle practices are, like all habits, routines of behavior that are repeated regularly and become customary and we had data at two time points – at enrollment and about 20 years previously. Like most studies reporting on the association of behavioral factors and dementia risk, our investigation is an observational study. In such studies unrecognized confounders or bias may account for the observed results and we cannot determine cause and effect. Our study has several strengths including the advantage of population-based prospective design with all subjects found to be dementia-free at baseline based on a clinical diagnosis of dementia using standard criteria. Routine and periodic reexamination of participants at short intervals (every 6-12 months) assured the identification of early cognitive changes and dementia.

Adherence to a healthful lifestyle throughout life has proven health benefits for several chronic diseases and is associated with reduced mortality. Although a healthful lifestyle may have helped our participants to reach the age of 90, lifestyle factors measured about 20 years previously were not associated with a lower risk of dementia after age 90. Of those lifestyle factors measured at enrollment in The 90+ Study, caffeine consumption, vitamin supplement intake and social/mental activities were related to lower risk in the oldest-old. These findings of a 30 to 45% decrease in risk could represent a substantial reduction in dementia incidence and warrant further study in other very old individuals.

Acknowledgements

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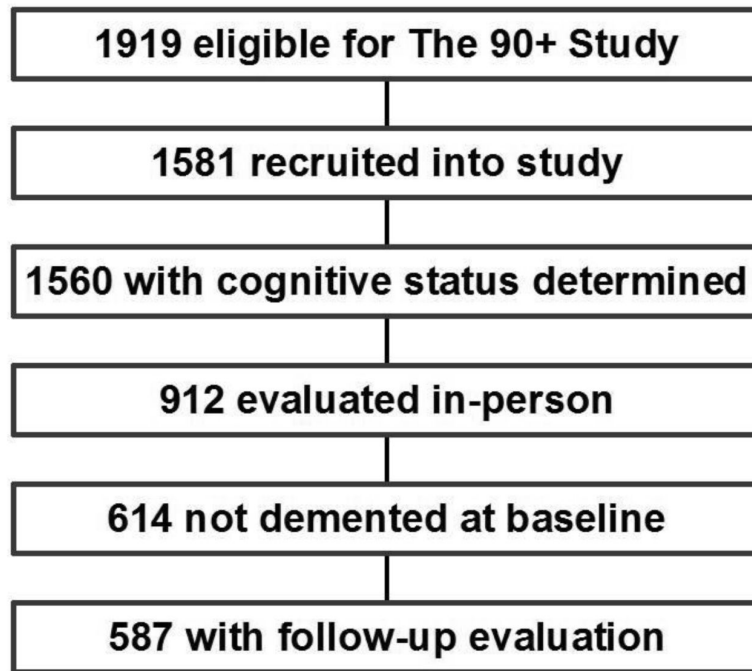
Figure 1.
Flow chart for selection of the 587 participants included in the analysis of lifestyle factors and risk of incident dementia

TABLE 1

Hazard ratios for incident dementia by lifestyle behaviors at enrollment in The 90+ Study and 20 years previously in the Leisure World Cohort Study

Lifestyle Behavior	At enrollment in The 90+ Study (2003 or later)				By the Leisure World Cohort Study (1980s)			
	No.[†]	No. with incident dementia	HR[‡]	95% CI	No.[†]	No. with incident dementia	HR[‡]	95% CI
Smoke								
Never	294	135	1.00		274	132	1.00	
Ever	271	119	0.95	0.74-1.21	313	136	0.84	0.66-1.07
<1 packs/day	156	70	0.95	0.71-1.28	160	71	0.80	0.60-1.07
1+ packs/day	99	39	0.89	0.62-1.27	144	61	0.90	0.66-1.22
Alcohol consumption (drinks/day)								
0	208	87	1.00		112	49	1.00	
<2	260	118	0.97	0.73-1.28	291	135	1.00	0.72-1.39
2+	79	41	1.09	0.75-1.58	184	84	1.03	0.72-1.46
Caffeine intake (mg/day)								
<50	104	52	1.00		147	61	1.00	
50-199	137	61	0.76	0.52-1.10	221	102	0.96	0.70-1.32
200+	97	41	0.66	0.43-0.99	219	105	1.04	0.76-1.43
Vitamin A supplements								
No	348	164	1.00		304	144	1.00	
Yes	239	104	0.77	0.60-0.98	283	124	0.90	0.71-1.15
Vitamin C supplements								
No	292	139	1.00		210	100	1.00	
Yes	295	129	0.74	0.58-0.94	377	168	0.92	0.72-1.19
Vitamin E supplements								
No	294	137	1.00		260	126	1.00	
Yes	293	131	0.74	0.58-0.95	327	142	0.86	0.67-1.10
Active exercise (hours/day)								
0	110	43	1.00		128	48	1.00	
<1	65	19	0.68	0.40-1.17	176	90	1.27	0.89-1.80
1+	67	25	0.80	0.49-1.32	282	130	1.16	0.83-1.62
DK	345	181	0.91	0.64-1.29				
Other exercise (hours/day)								
<3	120	46	1.00		147	63	1.00	
3-4	69	26	0.89	0.54-1.44	194	88	1.03	0.74-1.43
5+	52	15	0.69	0.39-1.24	244	117	1.15	0.84-1.57
DK	346	181	0.94	0.67-1.32				
Vigorous exercise at age 40								

Lifestyle Behavior	At enrollment in The 90+ Study (2003 or later)				By the Leisure World Cohort Study (1980s)			
	No.[†]	No. with incident dementia	HR[‡]	95% CI	No.[†]	No. with incident dementia	HR[‡]	95% CI
No					275	128	1.00	
Yes					175	79	1.12	0.84-1.50
Vigorous exercise in 1983 (hours/day)								
1					145	70	1.00	
2+					198	91	0.81	0.58-1.12
Vigorous exercise in 1998 (hours/day)								
1					137	54	1.00	
2+					144	63	1.22	0.83-1.78

[†] Numbers do not always total 587 due to subjects with missing values.

[‡] Adjusted for age by using age (continuous) as the time scale and for sex and education (high school, vocational school or some college, college graduate) by including as covariates in the model.

DK = Don't know; included as a separate category due to the large number with missing values.

TABLE 2

Hazard ratios for incident dementia by activities reported at enrollment in The 90+ Study

Activity / frequency	No.[†]	No. with incident dementia	HR[‡]	95%CI
Being outside, going for walks, enjoying nature				
< Daily	269	104	1.00	
Daily	248	119	1.01	0.78-1.32
Being with animals				
Rarely/never	328	156	1.00	
More frequently	176	62	0.67	0.50-0.90
Getting together with family and friends				
<= few times/month	198	90	1.00	
>= few times/week	319	134	0.92	0.70-1.21
Talking to family and friends on the phone				
<= few times/month	291	125	1.00	
>= few times/week	225	98	1.06	0.81-1.38
Going to movies, museums, entertainment				
Rarely/never	202	100	1.00	
More frequently	315	122	0.63	0.48-0.82
Going to church, synagogue, religious events				
Rarely/never	254	110	1.00	
More frequently	259	112	0.87	0.67-1.14
Shopping for groceries, clothes, etc.				
<= Monthly	132	68	1.00	
>= few times/month	387	155	0.53	0.39-0.70
Going for a ride in the car				
<= Monthly	145	75	1.00	
>= few times/month	365	143	0.71	0.53-0.94
Reading or having stories read				
< Daily	119	60	1.00	
Daily	397	165	0.74	0.54-0.99
Watching TV or listening to radio				
< Daily	30	15	1.00	
Daily	497	214	0.62	0.36-1.06
Doing vigorous exercise				
Rarely/never	265	106	1.00	
More frequently	247	113	0.88	0.67-1.16
Playing games or cards, doing crosswords, puzzles				
Rarely/never	371	169	1.00	
More frequently	150	55	0.78	0.57-1.05

Activity / frequency	No.[†]	No. with incident dementia	HR[‡]	95%CI
Doing handiwork or crafts				
Rarely/never	351	152	1.00	
More frequently	75	31	0.66	0.44-0.97
Gardening				
Rarely/never	474	205	1.00	
More frequently	39	14	0.76	0.44-1.31
Traveling with at least one overnight stay				
Rarely/never	300	130	1.00	
More frequently	213	91	0.82	0.63-1.08
Sitting and thinking				
< Daily	157	64	1.00	
Daily	354	156	0.91	0.68-1.22

[†] Numbers do not always total 587 due to subjects with missing values.

[‡] Adjusted for age by using age (continuous) as the time scale and for sex and education (high school, vocational school or some college, college graduate) by including as covariates in the model.