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Current alcohol consumption and its relationship to incident dementia: results from a 3-year follow-up study among primary care attenders aged 75 years and older

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Abstract

Objective: to investigate prospectively the relationship between current alcohol consumption (quantity and type of alcohol) and incident overall dementia and Alzheimer dementia.

Method: the study is based on individuals (75+) attending general practitioners in Germany: 3,202 subjects free of dementia were studied at baseline, 1.5 years and 3 years later by means of structured clinical interviews including detailed assessment of current alcohol consumption and DSM-IV dementia diagnoses. Associations between alcohol consumption (in grams of ethanol), type of alcohol (wine, beer, mixed alcohol beverages) and incident dementia were examined using Cox proportional hazard models, controlling for several confounders.

Results: incident overall dementia occurred in 217 of 3,202 participants over a mean follow-up period of 3 years. Significant relationships were found between alcohol consumption (prevalence at baseline: 50.0%) and incident overall dementia (adjusted hazard ratio (HR) 0.71, 95% CI 0.53–0.96), respectively, incident Alzheimer dementia (adjusted HR 0.58, 95% CI 0.38–0.89). With regard to quantity of alcohol and type of alcohol, all hazard ratios were found to be lower than 1.

Conclusion: in agreement with meta-analyses that include younger age groups, our study suggests that light-to-moderate alcohol consumption is inversely related to incident dementia, also among individuals aged 75 years and older.

Keywords: incident dementia, alcohol consumption, prospective longitudinal study, elderly

Introduction

There is no doubt that long-term alcohol abuse is detrimental to memory function and can cause neurodegenerative disease. Estimates from various studies have suggested the prevalence of alcohol-related dementia to be about 10% of all cases of dementia [1]. On the other hand, there is evidence that light-to-moderate alcohol consumption may decrease the risk of cognitive decline or dementia. A meta-analysis based on 23 longitudinal studies of subjects aged 65 years and older [2] suggests that the impact of small amounts of alcohol was associated with lower incidence rates of overall dementia (risk ratio (RR): 0.63; 95% CI 0.53–0.75) and Alzheimer dementia (RR: 0.57; 0.44–0.74) but not of vascular dementia (RR: 0.82; 95% CI 0.50–1.35) and cognitive decline (RR: 0.89; 0.50–1.35). The protective effect of light-to-moderate alcohol consumption may be due to a number of direct and indirect mechanisms: increased serum concentration of high-density lipoprotein; lowering of cholesterol; beneficial effects on platelet function, clotting and fibrinolysis and improved insulin sensitivity. The non-alcoholic components may have antioxidant, anti-inflammatory and vaso-relaxant properties [1]. It is still an open question whether different alcoholic beverages, such as beer, wine and spirits, have a similar effect. Some studies have shown a positive effect of wine only, which may be due either to the level of ethanol, the complex mixture that comprises wine or to the healthier life-style ascribed to wine drinkers [3].

In German-speaking countries, no data are available on the relationship between alcohol consumption and incident dementia. It is unknown whether the associations reported in meta-analyses that include subjects under the age of 75 can also be found for subjects developing dementia beyond the age of 75. Beyond this age, the vast majority of incident cases of dementia are identified [4].

Based on a large sample of non-demented primary care attenders (age 75+), the objective of this study is to reveal the relationship between alcohol consumption (including quantity and type of alcohol) and incident overall dementia and Alzheimer dementia.

Methods

Study design and sample

The sample consists of all subjects participating in the baseline assessment of a prospective longitudinal study on early detection of dementia in primary care. The study was conducted in six centres (Bonn, Düsseldorf, Hamburg, Leipzig, Mannheim and Munich) representing an urban area of cities with a total population ranging between about 300,000 (Mannheim) and almost 1.8 million (Hamburg). Altogether 138 GPs participated in the recruitment process. Inclusion criteria for GP patients were an age of 75 years and over, at least one contact with the GP within the last 12 months, and the absence of dementia in the GP's view. In order to identify dementia cases, the GPs used a

screening instrument with good psychometric properties [5]. Information on sampling frame, eligible subjects and respondents is given in Figure 1.

At baseline, a total of 3,327 patients were interviewed in their homes by trained investigators (physicians, psychologists, gerontologists) and reassessed 1.5 years and 3 years later. Information on the cognitive status of those who had died in the interim was collected from family members, caregivers or primary care physicians. Through linkage with primary care physicians the entire cohort was continuously monitored for morbidity and mortality.

Among the 3,327 patients interviewed at baseline, 84.8% ($n = 2,820$) could be personally interviewed 1.5 years later and 73.9% ($n = 2,460$) 3 years later. For the vast majority of subjects who could not be personally interviewed, systematic assessments (follow-up 1: 482; follow-up 2: 336) focusing particularly on dementia could be obtained from GPs, relatives or caregivers. Within 3 years, follow-up assessments were not available for only 49 subjects (1.5%). Proxy information could be obtained for 98.0% ($n = 295$) of the 301 patients who had died in the interim. Since dementia is associated with a higher mortality rate, proxy information is particularly important in order to avoid underestimation of incident dementia cases.

Instruments

To assess the *current use of alcohol*, participants were asked the following question: ‘At present, on how many days per week do you drink alcohol?’ (answer: never/1–2 days/3–4 days/5–6 days/7 days/I do not know). Those subjects who consumed alcohol were then asked ‘When you drink, how much alcohol do you drink on average?’ Frequency of alcohol consumption and quantity of beer, wine and liquor were determined. Data on alcohol intake were converted to a uniform measure of grams per day. Regardless of container size or alcohol type (i.e. beer, wine or spirits), one standard drink is any drink containing 10 g of alcohol. In this study, we distinguished between *quantity of alcohol consumption* (abstinent/1–9 g/10–19 g/20–29 g/30–39 g/40 or more grams) and *type of alcohol* (abstinent/wine (only)/beer (only)/mixed: wine, beer and other alcoholic beverages).

To assess *current nicotine consumption*, participants were asked whether at present they smoke cigarettes, a pipe, cigars or other tobacco products (yes/no/I do not know).

Diagnostic assessment of dementia was based on the Structured Interview for Diagnosis of Dementia of Alzheimer type, Multi-infarct Dementia and Dementia of other Aetiology according to DSM-III-R, DSM-IV and ICD-10 [6].

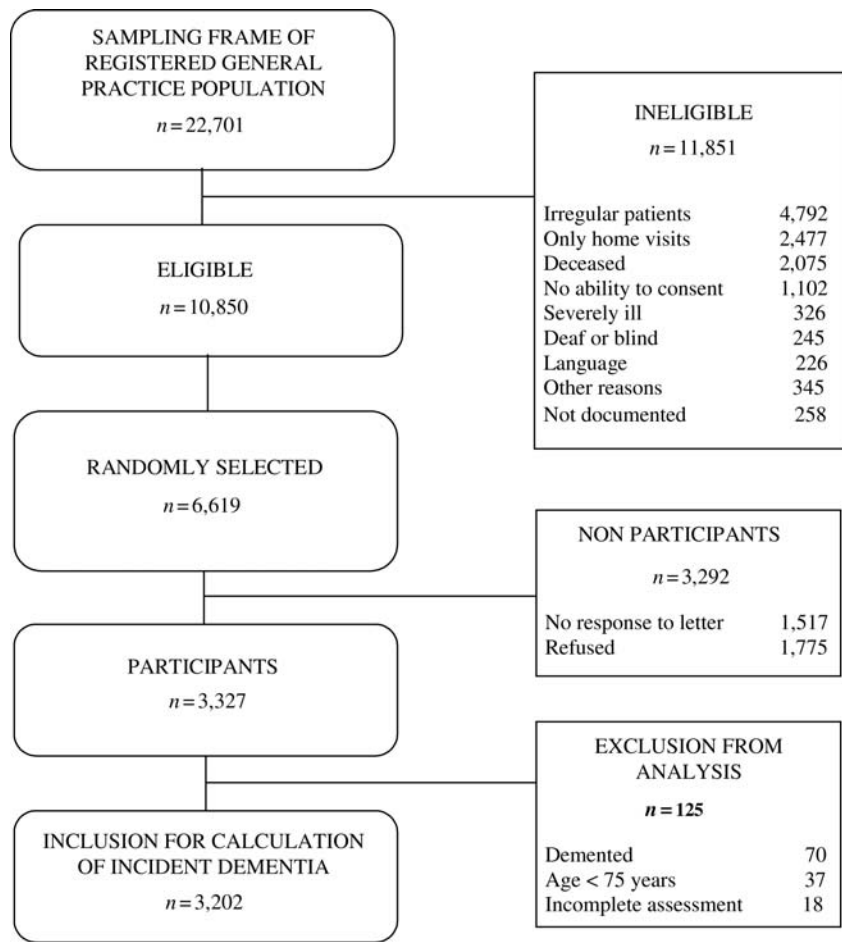


Figure 1. Sampling frame and sample.

Mild cognitive impairment (MCI) was diagnosed according to new consensus criteria proposed by the International Working Group on MCI [7–9].

Depressive symptoms were assessed by means of the 15-item short version of the Geriatric Depression Scale (GDS); [10, 11]. This instrument has good psychometric properties, also for German-speaking populations [12]. A cut-off point of 6 or more is commonly used to indicate depression.

A well-established 8-item-scale was used to measure *Instrumental Activities of Daily Living (IADL)* [13]. Subjects with an impairment in one of the eight items of the scale were regarded as impaired.

For each study participant his or her general practitioner (GP) filled out a questionnaire asking for *co-morbidity*. Based on this information, somatic co-morbidity was defined: no co-morbidity/1–4 diagnoses/5+ diagnoses.

For DNA analysis, leucocyte DNA was isolated with the Qiagen blood isolation kit according to the instructions of the manufacturer (Qiagen, Hilden, Germany). *Apolipoprotein E (apoE) genotyping* was performed according to standard procedures [14]. In analyses, subjects were divided into those with at least one 4 allele and those without an 4 allele.

Statistical analyses

The data were entered in the centres via an internet-based Remote-Data-Entry-System into a central ORACLE, version 9, database. The statistical analyses were performed with SPSS for Windows, version 15.0, and Statistical Analysis System (SAS), version 9.1. Prevalence rates of alcohol drinking were estimated as the percentage of the completely assessed non-demented subjects aged 75 years and over. Cox proportional hazard regression models (univariate and multivariate) were applied to examine the relationship between alcohol consumption and incident overall dementia and Alzheimer dementia. In the multivariate model, the following variables were entered: sex, age, education, living situation, IADL impairment, somatic co-morbidity, depression, apoE4 status, MCI and smoking. In all analyses, a *P*-value <0.05 was considered statistically significant.

Ethical approval

The Ethics Committees of the participating centres approved the study. Written informed consent was obtained from all participants.

Results

At baseline there were 3,202 persons without dementia. Information on current alcohol consumption was available for 3,180 subjects (Table 1): 50.0% were abstinent, 24.8%

Table 1. Prevalence of current alcohol consumption by socio-demographic characteristics and health indicators

Characteristic	Current alcohol consumption ^a % (n)	P-value (chi ²)
All subjects	50.0 (1,591/3,180)	—
Sex		
Male	73.5 (808/1,100)	<0.001
Female	37.6 (783/2,080)	
Age		
75–79	52.7 (895/1,698)	<0.001
80+	47.0 (696/1,482)	
Level of education (CASMIN) [26]		
Low	45.1 (887/1,966)	<0.001
Middle	53.6 (467/871)	
High	69.0 (237/343)	
Living alone		
Yes	40.1 (652/1,625)	<0.001
No	60.4 (939/1,555)	
Functional impairment [13]		
Impaired	48.8 (117/240)	0.688
Not impaired	49.8 (1,474/2,940)	
Somatic co-morbidity		
No somatic co-morbidity	54.0 (121/224)	0.413
1–4 somatic diagnoses	49.5 (1,107/2,235)	
5 and more somatic diagnoses	50.7 (356/702)	
Depression		
Yes (GDS-score 6+)	39.0 (115/295)	<0.001
No (GDS-score 0–5)	51.2 (1,475/2881)	
Mild cognitive impairment		
Yes	50.7 (240/473)	0.765
No	50.0 (1,351/2,704)	
Current smoking		
Yes	53.2 (126/237)	0.345
No	49.8 (1,465/2,943)	
apoE4		
Yes	48.3 (307/636)	0.265
No	50.8 (1,231/2,423)	

^aNo information on alcohol consumption (at baseline) available, *n* = 22.

12.8% 10–19 g and 12.4% 20 or more grams. A small subgroup of 25 participants fulfilled the criteria of harmful drinking (>60 g of alcohol per day for men, respectively, >40 g for women). One man (>120 g of alcohol per day) and one woman (>80 g of alcohol per day) reported an extremely high consumption of alcohol.

Among the consumers of alcohol almost half (48.6%) drank wine only, 29.0% drank beer only and 22.4% drank mixed alcohol beverages (wine, beer or spirits).

Alcohol consumption was significantly associated with male gender, younger age, higher level of education, not living alone and not being depressed. No association was found between alcohol consumption and functional impairment, somatic co-morbidity, smoking, MCI or apoE4 status.

The calculation of incident cases of dementia is based on 3,202 subjects who had no dementia at baseline. Within the follow-up period of 3 years, 217 cases of dementia (6.8%) were diagnosed, whereby 111 subjects (3.5%) suffered from Alzheimer dementia. Owing to the relatively

Table 2. Univariate and fully adjusted^a associations of current alcohol consumption (at baseline), quantity and type of current alcohol consumption with incident overall dementia and Alzheimer dementia

Current alcohol consumption	Univariate HR (95% CI) P-value	HR fully adjusted (95% CI) P-value
Incident overall dementia		
Abstinent	1 (referent group)	1 (referent group)
Not abstinent	0.62 (0.47–0.82) <0.001	0.71 (0.53–0.96) 0.028
Incident Alzheimer dementia		
Abstinent	1 (referent group)	1 (referent group)
Not abstinent	0.48 (0.32–0.71) <0.001	0.58 (0.38–0.89) 0.013
Quantity of current alcohol consumption (at baseline)		
Incident overall dementia		
Abstinent	1 (referent group)	1 (referent group)
1–9 g	0.70 (0.50–0.98) 0.036	0.76 (0.53–1.07) 0.118
10–19 g	0.63 (0.40–0.99) 0.045	0.78 (0.49–1.25) 0.296
20–29 g	0.37 (0.17–0.80) 0.011	0.40 (0.17–0.94) 0.034
30–39 g	0.58 (0.22–1.57) 0.285	0.72 (0.26–1.97) 0.517
40+ g	0.51 (0.19–1.39) 0.189	0.51 (0.16–1.64) 0.258
Incident Alzheimer dementia		
Abstinent	1 (referent group)	1 (referent group)
1–9 g	0.54 (0.33–0.88) 0.013	0.61 (0.36–1.01) 0.056
10–19 g	0.55 (0.29–1.04) 0.066	0.72 (0.37–1.39) 0.326
20–29 g	0.09 (0.13–0.67) 0.019	0.13 (0.02–0.95) 0.045
30–39 g	0.26 (0.04–1.86) 0.179	0.33 (0.05–2.41) 0.274
40+ g	0.67 (0.21–2.13) 0.497	0.68 (0.16–2.90) 0.606
Type of current alcohol consumption (at baseline)		
Incident overall dementia		
Abstinent	1 (referent group)	1 (referent group)
Wine (only)	0.66 (0.47–0.93) 0.017	0.79 (0.55–1.13) 0.196
Beer (only)	0.77 (0.52–1.15) 0.197	0.87 (0.56–1.35) 0.528
Mixed (wine, beer and other alcoholic beverages)	0.35 (0.19–0.65) 0.001	0.35 (0.17–0.69) 0.003
Incident Alzheimer dementia		
Abstinent	1 (referent group)	1 (referent group)
Wine (only)	0.61 (0.38–0.97) 0.035	0.76 (0.46–1.23) 0.259
Beer (only)	0.50 (0.27–0.94) 0.032	0.60 (0.30–1.21) 0.152
Mixed (wine, beer and other alcoholic beverages)	0.17 (0.05–0.54) 0.003	0.14 (0.03–0.56) 0.006

^aFor sex, age, education, living situation, IADL impairment, somatic co-morbidity, depression, apoE4, MCI and smoking.

small numbers, other subgroups of dementia (vascular dementia: $n = 42$; other specific dementia, e.g. dementia in Parkinson's disease, Lewy body dementia, alcohol dementia: $n = 14$; dementia with unknown aetiology: $n = 50$) were not considered in the following analyses.

Univariate and multivariate analyses revealed that alcohol consumption was significantly associated with a lower incidence of overall dementia and Alzheimer dementia (Table 2). Additional calculations excluding initial MCI subjects and those who died in the interim revealed very similar results.

With regard to quantity of alcohol, all hazard ratios were found to be lower than 1; a statistically significant association, however, was found only for subjects consuming between 20 and 29 g of alcohol per day.

Hazard ratios for all types of alcohol were found to be lower than 1, with statistically significant hazard ratios found among those drinking mixed alcoholic beverages.

Discussion

Persons who continue drinking alcohol throughout old age are the remainder population, exhibiting a survivor

phenomenon. In line with a large-scale study also based on GP attenders aged 75 years and older [15], we found that light-to-moderate alcohol consumption was associated with relatively good physical and mental health.

Comparisons with other epidemiological studies on the impact of alcohol on dementia are difficult for various reasons: age of the subjects, the length of follow-up and the endpoints studied, the definition of quantity and type of alcohol consumption and the covariates considered. Follow-up length in studies on the association between alcohol and incident dementia varied from 1 to 25 years, with most studies having more than 5 years of follow-up [2]. Since our 3-year follow-up study included, at baseline, only those subjects 75 years of age and older, the mean age of our sample was, at 80.2 years, much higher than that in most studies.

Among the strengths of this study are its large size and the ability to control for social factors, physical and mental health and lifestyle-related (i.e. smoking) or genetic (i.e. apoE4 status) factors. Alcohol consumption was significantly associated with factors that are protective for the development of dementia: better education, not living alone and absence of depression. Even after controlling for these

and several other factors, the risk for incident dementia was still significantly lower among light-to-moderate alcohol consumers. Another advantage is the systematic proxy assessment of dementia in deceased or unavailable participants; however, due to limited information in most of these cases, no specific dementia diagnosis could be made.

Based on a follow-up period of 3 years, incidence rates of overall dementia (6.8%) and Alzheimer dementia (3.5%) were substantial. With an almost complete identification of incident dementia cases—also of those subjects who died in the interim—we found that alcohol consumption at baseline is significantly associated with lower incidence of overall dementia and Alzheimer dementia. This is in line with the results of a comprehensive meta-analysis [2], which is mainly based on subjects under the age of 75. Our result that light-to-moderate consumption is significantly related to incident dementia among the old—old is supported by a study that reported similar associations of alcohol use with odds of dementia among subjects aged 80–89 years and subjects aged 70–79 years [16].

With regard to quantity of alcohol and dementia, all hazard ratios were lower than 1; a statistically significant association, however, was found only for subjects with either incident overall dementia or incident Alzheimer dementia consuming between 20 and 29 g of alcohol. Our results are roughly consistent with the findings of two large-scale studies [16, 17]: in the Rotterdam Study [17], taking 1–3 drinks per day was found to be significantly associated with a reduced risk of all dementias [17]. The Cardiovascular Health Study [16] reported that compared with abstention, the adjusted odds for dementia among those whose weekly alcohol consumption was less than 1 drink were 0.65 (95%CI: 0.41–1.02); 1–6 drinks, 0.46 (95%CI: 0.27–0.77); 7–13 drinks, 0.69 (95%CI: 0.37–1.31); and 14 or more drinks, 1.22 (95%CI: 0.60–2.49) [16].

Hazard ratios for all types of alcohol were found to be lower than 1, with statistically significant hazard ratios found among those drinking mixed alcoholic beverages. In the Rotterdam Study [16] also there was no evidence found that the relation between alcohol and incident dementia varied by type of alcohol beverage. In the Cardiovascular Health Study, the association of beer, wine or liquor consumption with incident dementia was tested [16]. The three beverage types did not differ significantly in their relationships to dementia. In contrast to this, other longitudinal studies in Göteborg [3], New York City [18], Copenhagen [19], Canada [20] and France [21, 22] found that only the consumption of wine was associated with lower rates of overall dementia, respectively, Alzheimer dementia.

In a rigorously conducted randomised controlled trial, direct causal inferences can be made from the effects observed. Since it would be neither ethical nor practically feasible to carry out a randomised controlled trial with alcohol as a dose-controlled intervention, an observational study is the only alternative. Compared with case-control

studies and historical cohort studies, prospective longitudinal studies provide information at a much lower risk of bias.

However, there are also several limitations of our study. A number of factors may have influenced the findings and should be considered when interpreting the results: since only about 50% of the randomly selected patients consented to participate in the study, selection bias might play a role. The study excluded older people in nursing homes, as well as patients who were unable to attend the practice of a primary care physician. Alcohol consumption is self-reported and its accuracy may thus be questioned. In general, self-reports of alcohol consumption are taken to be valid for the purposes of classifying substance users into broad consumption bands [23, 24]. The method used in this study to ascertain alcohol consumption includes questions about the frequency of consumption and the amount consumed for beer, wine and liquor separately, and has been reported to yield the most realistic levels of intake [25]. Counting standard drinks is a more reliable measure of how much alcohol is consumed than counting either glasses or bottles. The inclusion of ex-drinkers together with never drinkers in the non-drinker category places some reservations on the observed findings. However, due to the high mortality rate of persons with a history of alcoholism, the number of such persons in our study is probably low.

Although the consumption of alcohol decreases with increasing age, in Germany the current use of alcohol among the elderly is substantial (men: 73.5%; women: 37.6%). Our study suggests that light-to-moderate alcohol consumption is inversely related, also among subjects aged 75 years and older, to both incident overall dementia and incident Alzheimer dementia. Although alcohol consumption was related to less incident dementia, this may not be a causal relationship. It could be that participants who drank alcohol sensibly also have a healthier lifestyle in terms of physical, dietary and mental perspectives.

Key points

- Among a large sample of individuals (75 years of age and older) without dementia at baseline, 50% consumed alcohol, in general less than 2 drinks per day.
- Persons who continue drinking alcohol throughout old age are the remainder population, exhibiting a survivor phenomenon.
- After controlling for a number of potential confounders current alcohol consumption was associated with a 29% decrease in overall dementia incidence (respectively, a 42% decrease in Alzheimer dementia).
- With regard to quantity of alcohol and type of alcohol, all hazard ratios were found to be lower than 1.

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Conflicts of interest

None declared.

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Limitations in physical functioning among older people as a predictor of subsequent disability in instrumental activities of daily living

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Abstract

Background: physical functioning describes the underlying abilities that make activities necessary for independent living in the community possible.