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Cardiovascular risk factors and cognitive decline in adults aged 50 and over: a population-based cohort study

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Abstract

Objectives: the objective of the present study was to explore the association between cardiovascular risk and cognitive decline in adults aged 50 and over.
Methods: participants were older adults who participated in the English Longitudinal Study of Ageing. Outcome measures included standardised z-scores for global cognition, memory and executive functioning. Associations between cardiovascular risk factors and 10-year Framingham risk scores with cognitive outcomes at 4-year and 8-year follow-ups were estimated.
Results: the mean age of participants ($n = 8{,}780$) at 2004–05 survey was 66.93 and 55% were females. Participants in the highest quartile of Framingham stroke risk score (FSR) had lower global cognition ($b = -0.73$,CI: −1.37, −0.10), memory ($b = -0.56$, CI: −0.99, −0.12) and executive ($b = -0.37$, CI: −0.74, −0.01) scores at 4-year follow-up compared with those in the lower quartile. Systolic blood pressure ≥160 mmHg at 1998–2001 survey was associated with lower global cognitive ($b = -1.26$, CI: −2.52, −0.01) and specific memory ($b = -1.16$, CI: −1.94, −0.37) scores at 8-year follow-up. Smoking was consistently associated with lower performance on all three cognitive outcomes.
Conclusion: elevated cardiovascular risk may be associated with accelerated decline in cognitive functioning in the elderly. Future intervention studies may be better focused on overall risk rather than individual risk factor levels.

Keywords: *cognition, vascular factors, risk score, prospective study, older people*

Introduction

Cognitive decline becomes more common with ageing and, for an increasing number of people, interferes with daily functioning and well being. Several cardiovascular (CVD) risk factors, including high blood pressure (BP), dyslipidaemia, smoking and obesity, have been proposed as important modifiable risk factors for cognitive decline [1, 2]. Longitudinal studies that explored the association of vascular risk factors with cognitive functioning produced contradictory or inconclusive findings reporting positive, negative and absent relationships between BP [1, 3–5], serum cholesterol [1, 6–8] and BMI [9, 10] with cognitive functioning. There is more consistent evidence that smokers tend to be at a greater risk of cognitive decline compared with non-smokers [11] although the risk might be limited to specific cognitive domains [9, 12]. Considering composite measures of risk, cross-sectional studies [13, 14] tend to report associations between higher Framingham stroke risk (FSR) scores and worse cognitive function, including a recent study of UK civil service employees by Kaffashian *et al.* [15]. However, no population-based longitudinal evidence is available to date on this exposure.

The aim of the analyses described here was to investigate the prospective associations of FSR and CVD risk scores (FCVDR), BP, cholesterol levels, smoking and BMI in relation to cognitive function in a nationally representative sample of adults. A particular objective was to explore the extent to which the association of vascular risk factors with cognitive decline varied as a function of the length of follow-up. The focus was on predictors with greatest opportunities for intervention: specifically, BP, cholesterol, smoking and BMI.

Methods

The study employed data from the English Longitudinal Study of Ageing (ELSA) which is a prospective and

nationally representative sample of people aged 50 and over residing in private households in England. To date there are five data collection surveys (1998–2001, 2002–03, 2004–05, 2006–07, 2008–09) and the present analyses drew primarily on 2004–05 data ($n = 9,432$) which represent the first survey where both cognitive and physiological measurements, including systolic blood pressure (SBP), cholesterol levels and BMI, were collected. Out of the 8,780 core study members, 6,269 (71%) also contributed data to the 2008–09 follow-up (see Supplementary data available in *Age and Ageing* online, Appendix 1). Biomedical and physical performance measures were collected from respondents by a trained nurse on 7,666 core members. Full details on response to the main interview and physiological measurements are provided in the Technical Report [16]. Data from the 1998–2001 survey ($n = 11,205$) were also incorporated. About 6,981 (62%) have also participated in the 2008–09 follow-up study.

Cognitive measures

Memory

Each respondent was asked to learn 10 unrelated words, and immediate and delayed recall were tested (the delayed recall performed after the letter-cancellation and animal-naming tests). Immediate and delayed recall tests have been shown to have good construct validity and consistency [17]. For the prospective memory test, the respondents had to remind the interviewer to do two-specific tasks at the end of the test. A memory index was created by summing-up the z-scores on the individual memory tests.

Executive functioning

A verbal fluency task involved the participants naming as many different animals as possible within 1 min. The reliability and validity of the animal-naming test is well documented [18]. A letter-cancellation test was used to measure attention, mental speed and visual scanning abilities with two-independent scores are calculated: speed and accuracy. An index of executive functioning was developed by summing-up the z-scores on animal naming, speed and accuracy tasks.

Cognitive index

A continuous measure of overall cognitive functioning was provided by summing-up participants' z-scores on the memory and executive indexes. Each test receives equal weighting towards the combined cognitive index.

Vascular risk factors

Blood pressure

BP measurements included SBP and DBP values assessed by the nurse at three surveys (1998–2001, 2004–05 and 2008–09) and were recorded on each occasion as the average of three measurements taken on the right arm with the informant in a seated position after 5 min rest. Finally, a categorical variable was created at both 1998–2001 and 2004–05 surveys that classified individuals into 'normal' (SBP <140 mmHg and DBP ≤90 mmHg), 'borderline-high' (SBP 140–160 mmHg and DBP >90–99 mmHg) and 'high' (SBP >160 mmHg and DBP ≥100 mmHg) [7].

Cholesterol

Measure of fasting serum cholesterol included total cholesterol levels. The continuous measure was developed in an identical fashion to that described for BP. The categorical variable aimed to classify respondents into what may be seen as clinically relevant categories. Thus, at both 1998–2001 and 2004–05 surveys according to their TC levels participants were classified as optimal (0–5.2 mmol/l), mildly high (5.2 to <6.2) and high (>6.2 mmol/l).

BMI

At each survey two BMI variables were developed following the BP and TC procedures. The categorical variable for BMI grouped participants into normal (18.5–25 kg/m^2), overweight (25–29.9 kg/m^2) and obese (≥30 kg/m^2).

Smoking

Participants were classified in two groups: non-smokers (never smoked or ex-smokers) and smokers (current smokers).

Cardiovascular risk profile

The study also used the FSR and FCVDR risk scores using 2004–05 data. These risk scores were calculated using information on age, gender, systolic blood pressure, ratio of TC to HDL, diabetes and cigarette smoking and follow the equations reported by Anderson *et al.* [19]. Left ventricular hypertrophy was not included as this information is not collected in ELSA. Risk scores were divided into quartiles for analysis.

Covariates

Additional variables known to be associated with both cognitive functioning and vascular disease were selected. Aside from age (continuous) and gender (binary), *highest educational qualification* grouped participants into: no qualification; level 1 National Vocational Qualification (NVQ1) or certificate of secondary education (CSE); NVQ2 or O-level; NVQ3 or A-level or higher qualification but below degree and degree-level or higher or NVQ 4/5. *Alcohol intake* was calculated from participant-reported drinking frequency over the previous year (weekly drinking versus occasional or never). Based on participant-reported frequency of physical activity a four

category *physical exercise* variable was created: sedentary, low, moderate and high. An abbreviated Center for Epidemiological Studies Depression Scale (CES-D) [20] measure was used to create a continuous measure of *depressive symptoms* (scores ranged from 0 to 8). As 1998–2001 data did not incorporate CES-D, the General Health Questionnaire (GHQ-12) [21] was used as a measure of current mental health status (scores ranging from 0 to 12). Self-reported stroke and diabetes (present/absent) were also included as covariates. The final covariates included whether or not respondents were treated with antihypertensive or cholesterol-lowering drugs (yes/no).

Statistical analysis

Descriptive statistics were estimated to determine the study sample characteristics. The primary analysis involved multivariable regression analysis using 2004–05 data to estimate the association of SBP, DBP, TC, smoking and BMI values with overall and specific cognitive decline at 4-year follow-up (2008–09 survey) adjusting for baseline (2004–05) covariates. Cognitive adjustment at baseline involved including the corresponding measure as a covariate, for instance when estimating memory at the follow-up baseline memory score was used as a covariate. The association of high and border-range SBP, DBP, TC and BMI values at 2004–05 surveys compared with normal-range values on overall and specific cognitive measures at 2008–09 follow-up was also estimated using the same estimation models. Similar estimation models were employed to predict the association of the same vascular risk factors assessed at the 1998–2001 survey with cognitive performance at 8-year follow-up (Figure 1).

In addition, multivariable linear regression analyses were used to investigate the longitudinal association between 10-year FSR and FCVDR scores quartile at 2004–05 survey with cognitive decline at 4-year follow-up, adjusting for baseline (2004–05) data. Participants in the bottom quartile of stroke and CVD risk scores distribution were used as the reference category. These analyses excluded participants with a diagnosis of CVD (angina, myocardial infarction, congestive heart failure and heart murmur), stroke or dementia at or prior to 2004–05 survey. As the results for men and women were similar, for ease of presentation the overall results are presented. A level of 0.05 was chosen to indicate statistical significance. All analyses were carried out using STATA version 11. Analyses were weighted to adjust for non-response.

Results

Table 1 shows the characteristics of the 1998–2001 and 2004–05 study samples. The mean age of participants was 62.5 at the 1998–2001 survey compared with 66.93 at the 2004–05 survey with 55% being females in both surveys. There was a modest decline in mean SBP values from the 1998–2001 (141.5 mmHg) to the 2004–05 (136.4 mmHg) surveys. Total cholesterol mean values were similar at the two surveys (6.0 and 5.9 mmol/l, respectively) as were

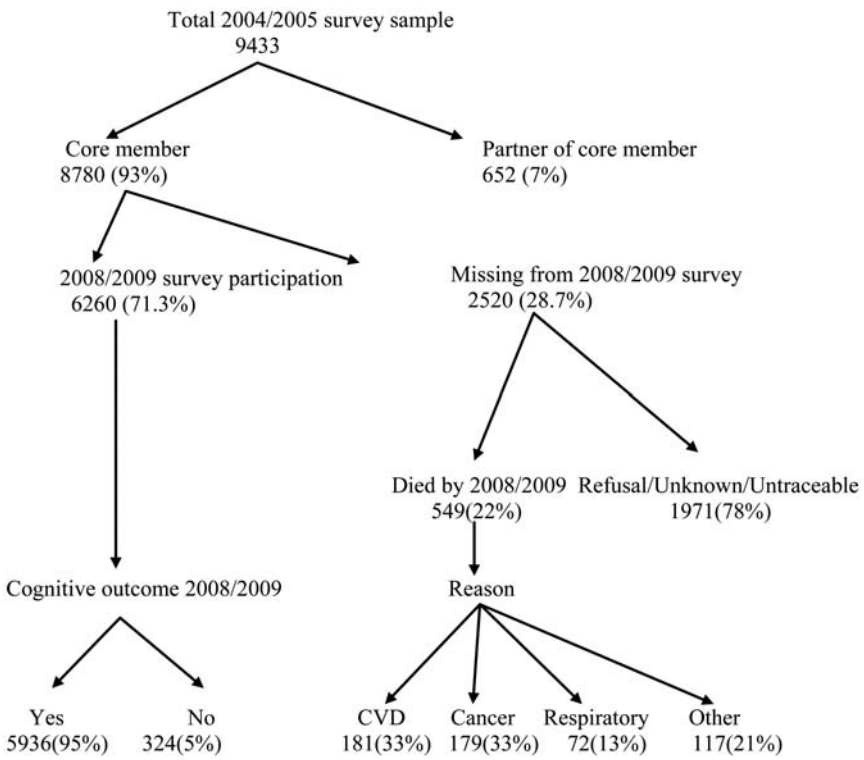

Figure 1. Diagram charting 2004–05 survey participants' response patterns at 2008–09 survey.

Table 1. Characteristics of participants at 1998–2001 and 2004–05 surveys

	1998–2000		2004–05	
	Freq.	Mean or %	Freq.	Mean or %
Age (years)	11,205	62.5	8,780	66.9 (10.1)
Sex				
Female	6,148	55	4,830	55
Male	5,057	45	3,950	45
Smoker (current versus never or past)				
No	9,032	81	7,424	85
Yes	2,170	19	1,329	15
Alcohol intake				
Never or occasionally	7,392	66	4,903	65
Weekly	3,792	34	2,696	35
BMI (continuous)	10,121	27.6 (4.6)	7,225	28.6 (5.2)
Qualifications				
No education—reference group	4,951	44	3,418	39
NVQ1/CSE/Other	1,455	13	1,197	14
NVQ2/GCE O level	1,754	16	1,465	17
NVQ3/A level/below degree	1,839	16	1,622	18
NVQ4/NVQ5/degree+	1,206	11	1,069	12
Physical exercise				
Low or sedentary	2,175	32	2,738	31
Moderate	3,188	46	4,356	50
Vigorous	1,521	22	1,588	19
Systolic blood pressure (continuous)	8,465	141.5 (19.6)	7,563	136.4 (19.1)
Diastolic blood pressure (continuous)	8,465	77.4 (12.1)	7,563	75.5 (11.2)
Total cholesterol (continuous)	3,867	6.0 (1.1)	5,904	5.9 (1.2)
HDL cholesterol (continuous)	4,026	1.5 (0.4)	5,899	1.5 (0.4)
LDL cholesterol (continuous)	169	3.7 (1.0)	5,742	3.6 (1.0)
Depression (continuous)	10,722	1.3 (2.5)	8,686	1.5 (2.0)
Blood pressure-lowering drugs				
No	5,171	66	7,467	85
Yes	2,621	34	1,313	15
Cholesterol-lowering drugs				
No	8,132	94	8,537	97
Yes	556	6	243	3
Stroke—doctor diagnosed				
No	11,047	99	8,314	95
Yes	158	1	466	5
Diabetes—doctor diagnosed				
No	10,692	91	8,000	91
Yes	513	5	780	9
Cognitive functioning index	NA	NA	8,370	28.5 (6.7)
Memory index	NA	NA	8,630	15.4 (4.5)
Executive functioning index	NA	NA	8,372	13.0 (3.4)
2008–2009 survey—cognitive outcomes				
Cognitive functioning index			5,350	28.6 (6.3)
Memory index			5,913	15.2 (3.9)
Executive functioning index			5,355	13.3 (3.4)

For categorical variables mean refers to the proportion of respondents. Missing cases are excluded.

mean BMI values (27.6 versus 28.5 kg/m^2). There was limited change in the mean scores on all cognitive outcome measures over time among participants taking part in both 2004–05 and 2008–09 data. For response patterns, see Supplementary data available in *Age and Ageing* online, Appendix 1. Table 2 shows the relationship between FSR and FCVDR quartile at 2004–05 survey with cognitive decline at 4-year follow-up. The results indicate that compared with participants in the lower quartile of FSR those in the upper quartile of FSR showed significantly lower overall cognitive ($b = -0.73$, $P < 0.05$), specific memory ($b = -0.56$, $P < 0.05$) and executive ($b = -0.37$, $P < 0.05$) scores at 4-year follow-up, even after adjusting for 2004–05 cognitive scores. Participants in the third quartile of FSR also presented lower overall cognitive ($b = -0.61$, $P < 0.05$) and specific memory ($b = -0.50$, $P < 0.05$) scores compared with those in the lower quartile. FCVDR score estimates were in the same direction and of similar size to the FSR scores.

The longitudinal associations between vascular risk factors and all three cognitive measures are shown in Table 3. To test the hypothesis for a duration–response

Table 2. Longitudinal association between 2004 and 2005 Framingham stroke risk (FSR) score with cognitive outcomes at 4-year follow-up

	Cognitive index *b* (95% CI)	Memory index *b* (95% CI)	Executive index *b* (95% CI)
FSR score quartiles (range)			
Lower quartile (0.005–0.038)	Reference	Reference	Reference
Second quartile (0.039–0.063)	0.06 (−0.34, 0.47)	−0.02 (−0.30, 0.27)	−0.03 (−0.27, −0.22)
Third quartile (0.064–0.106)	**−0.61 (−1.10, −0.12)**	**−0.50 (−0.84, −0.16)**	−0.23 (−0.52, 0.06)
Upper quartile (0.107–0.567)	**−0.73 (−1.37, −0.10)**	**−0.56 (−0.99, −0.12)**	**−0.37 (−0.74, −0.01)**
FSCVD score quartiles (range)			
Lower quartile (0.005–0.038)	Reference	Reference	Reference
Second quartile (0.039–0.063)	0.41 (−0.84, 0.02)	−0.23 (−0.52, 0.07)	−0.21 (−047, −0.06)
Third quartile (0.064–0.106)	**−0.72 (−1.234, −0.20)**	**−0.59 (−0.94, −0.24)**	−0.23 (−0.54, 0.07)
Upper quartile (0.107–0.567)	**−0.92 (−1.53, −0.31)**	**−0.56 (−0.99, −0.13)**	**−0.45 (−0.80, −0.08)**

The analyses also adjusted for gender, age, alcohol, physical activity level, educational qualifications, depression and cognitive functioning at 2004–05 survey. Bold figures indicate statistical significance at 0.05 level. Participants with past or present CVD at 2004–05 survey, stroke or dementia disease have been excluded from the estimation models.

effect with respect to the relationship between BP and cognitive decline, Table 3 includes the results based on 1998–2001 BP data (first column). The results revealed that smoking represents the most consistent vascular risk predictor of cognitive decline across all three cognitive outcomes in both models. High BMI was also associated with lower scores ($b = -0.02$, $P < 0.05$) on memory as was borderline high SBP levels ($b = -0.24$, $P < 0.05$). With respect to the 1998–2001 estimation model, the results revealed that both high DBP and SBP were associated with lower global cognitive and memory scores at 8-year follow-up. However, when BP was used as a categorical predictor the results indicating that SBP over 160 mmHg was negatively associated with lower overall cognitive ($b = -1.26$, $P < 0.05$) and memory ($b = -1.16$, $P < 0.05$) scores at 8-year follow-up.

Discussion

The present study investigated vascular risk factors for cognitive impairment in this informative longitudinal cohort. In a large prospective data, the study found that 10-year FSR and FSCVD were significantly associated with cognitive decline on both global and specific (memory and executive) measures at 4-year follow-up.

An important outcome of the present study was the consistent association observed between smoking and low global cognitive and specific memory and executive scores at 4-year and 8-year follow-ups. With respect to the association of BP with cognitive functioning, the findings imply that both age and probably duration of high BP levels are in the long-term detrimental to cognitive performance. For instance, participants in the 1998–2001 survey were on average 5 years younger than those in the 2004–05 suggesting that age, duration or both might be associated with declined cognitive performance. The possibility of a cumulative effect also seems probable whereby participants with high SBP (>160 mmHg) values were at a greater risk of lower cognitive scores 8 years later compared with those with normal SBP vales (<140 mmHg). Of note is the finding that participants with borderline high SBP levels at 2004–05 were at risk of lower memory scores 4 years later. It may be that individuals with borderline high SBP levels were not prescribed antihypertensive treatment drugs which then results in an increased risk of cognitive decline over the short term. This suggestion needs confirmation from future research. Overall, the study findings indicate that high BP may be detrimental to cognitive functioning and that this impact is likely to develop over a longer period of time, future clinical trials might benefit from this insight.

A domain-specific association of vascular risk factors seems also probable. Particularly, the detrimental association of BP appeared to be restricted to memory functioning. Alternatively, a longer exposure to high BP may be needed for a significant decline in executive performance to be observed. These suggestions are compatible with a *domino* effect whereby preliminary memory impairment as a result of high BP is later translated in impaired executive functioning performance. It is equally plausible to suggest that executive functioning decline over the short term presents a higher threshold that entails the combined association of multiple vascular risk factors.

The latter suggestion appears to be supported by the negative longitudinal association between FSR and FCVDR with all three cognitive outcome measures at 4-year follow-up. In particular, participants in the upper quartile of the stroke and CVD risk scores are at a greater risk of global cognitive as well as specific memory and executive decline relative to their counterparts in the lower quartile. These findings substantiate the claim that the combined effects of particular vascular risk factors may expedite the process of cognitive decline. It would appear that the most promising preventative approach would be one that considers the multicausality nature of cognitive decline. Specifically, interventions to limit cognitive decline should consider the combined effect of multiple vascular risk factors rather than focusing on the management of individual-risk factors as routinely performed in the past.

Table 3. Unstandardised coefficients (*b*) and confidence intervals (95% CI) for 1998–2001 and 2004–05 vascular risk predictors of cognitive outcomes at 2008–09 follow-up

	Cognitive index *b* (95%CI)		Memory index *b* (95%CI)		Executive index *b* (95%CI)	
	1998–2001	2004–05	1998–2001	2004–05	1998–2001	2004–05
Continuous predictors model						
SBP (mmHg)	**−0.22 (−0.43, −0.01)**	−0.04 (−0.15, 0.07)	**−0.16 (−0.29, −0.03)**	−0.04 (−0.12, 0.04)	−0.06 (−0.18, 0.06)	−0.01 (−0.07, 0.06)
DBP (mmHg)	**−0.31 (−0.59, −0.03)**	−0.05 (−0.23, 0.13)	**−0.20 (−0.38, −0.02)**	0.00 (−0.14, 0.09)	−0.10 (−0.26, 0.06)	−0.05 (−0.16, 0.05)
TC (mmol/l)	0.05 (−0.20, 0.29)	−0.04 (−0.21, 0.12)	−0.06 (−0.21, 0.10)	−0.02 (−0.14, 0.10)	0.13 (−0.01, 0.27)	−0.02 (−0.11, 0.08)
BMI (kg/m^2)	0.01 (−0.06, 0.07)	−0.01 (−0.05, 0.04)	−0.01 (−0.04, 0.04)	**−0.02 (−0.05, −0.01)**	0.01 (−0.02, 0.05)	0.01 (−0.01, 0.04)
Categorical predictors model						
SBP (mmHg), Ref: <140						
140 to <160	0.07 (−1.00, 1.15)	−0.31 (−0.64, 0.03)	−0.14 (−0.80, 0.51)	**−0.24 (−0.46, −0.01)**	0.27 (−0.33, 0.87)	−0.05 (−0.26, 0.16)
≥160	**−1.26 (−2.52, −0.01)**	−0.12 (−0.63, 0.38)	**−1.16 (−1.94, −0.37)**	−0.07 (−0.42, 0.28)	−0.27 (−0.96, 0.42)	−0.04 (−0.34, 0.26)
DBP (mmHg), Ref: <80						
80 to <90	−0.01 (−0.67, 0.67)	−0.13 (−0.45, 0.20)	−0.08 (−0.49, 0.34)	−0.03 (−0.25, 0.19)	0.11 (−0.39, 0.61)	−0.09 (−0.29, 0.11)
≥90	−0.60 (−1.51, 0.31)	0.09 (−0.41, 0.58)	−0.45 (−1.03, 0.16)	0.20 (−0.15, 0.54)	−0.24 (−0.93, 0.45)	−0.07 (−0.36, 0.22)
TC (mmol/l), Ref: <5.2						
5.2<6.20	−0.30 (−0.97, 0.37)	0.22 (−0.17, 0.62)	−0.26 (−0.67, 0.15)	0.06 (−0.20, 0.33)	−0.13 (−0.52, 0.26)	0.18 (−0.06, 0.42)
≥6.2	0.08 (−0.56, 0.73)	−0.02 (−0.40, 0.36)	−0.21 (−0.61, 0.20)	−0.05 (−0.30, 0.20)	0.33 (−0.04, 0.71)	0.02 (−0.21, 0.26)
BMI (kg/m^2), Ref: <25						
Overweight (25−29.99)	−0.25 (−0.89, 0.38)	−0.02 (−0.37, 0.32)	−0.29 (−0.68, 0.11)	−0.05 (−0.28, 0.19)	0.03 (−0.34, 0.39)	0.02 (−0.23, 0.18)
Obese (≥30)	−0.01 (−0.79, 0.77)	0.04 (−0.40, 0.36)	−0.12 (−0.60, 0.37)	−0.12 (−0.40, 0.16)	0.15 (−0.29, 0.59)	0.06 (−0.17, 0.28)
Current smoker (yes/no)	**−1.51 (−2.29, −0.74)**	**−0.44 (−0.88, −0.01)**	**−0.70 (−1.19, −0.21)**	−0.23 (−0.52, 0.07)	**−0.87 (−1.31, −0.43)**	**−0.29 (−0.55, −0.03)**

Bold figures indicate statistical significance at 0.05 level. The estimation models also adjusted for gender, age, alcohol, educational qualifications, depression, stroke, diabetes, BP and cholesterol-lowering drugs and cognitive functioning. SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; BMI, body mass index; CI, confidence interval.

Present findings corroborate with earlier evidence that the negative association of BP with cognitive functioning represents a gradual process that takes place over long periods of time [4, 22, 23]. The limited evidence of an association between BP and cognitive decline at 4 year may explain the lack of significant effect of short-term antihypertensive clinical trials with cognitive decline [24–26]. A detrimental association of smoking with cognitive functioning at midlife has been reported previously [27] and the present extend these findings to older people within a population-based cohort data. Finally, the study findings extend previous cross-sectional [13] studies and confirm longitudinal evidence [14] for a negative association between FSR and FCVDR risk scores with cognitive impairment in adults.

The present data have many strengths including the use of both individual and combined vascular risk factors, different follow-up periods, the ability to adjust for prior cognitive functioning (important limitation of previous studies), the longitudinal design and its representativeness. Several limitations are also important to mention. The present data did not collect information on cognitive functioning at 1998–2001 survey which impeded our ability to tests similar models. However, the 1998–2001 estimation model included an educational qualifications measure, a commonly employed proxy measure for cognitive functioning. Further, present data include only two surveys with both cognitive functioning and physiological measures of vascular risk factors which limited our ability to model the relation between vascular risk factors and cognitive functioning over time. This issue remains to be tested.

The present study adds new knowledge by documenting a longitudinal association between FRS and CVD risk scores with both global and specific cognitive decline. Regarding particular vascular risk factors, smoking emerged as the most consistent predictor of cognitive decline. The relationship between BP with cognitive functioning appears to be time-dependent supporting a possible duration–response effect. These findings could serve as basis on which to develop future clinical trials aimed at preventing atypical cognitive decline in adults aged 50 and over and for designing population-level interventions.

Key points

- Population-based evidence on the influence of multiple vascular risk factors on cognitive decline in elderly is scarce and inconclusive.
- The combined effects of particular vascular risk factors may expedite the process of cognitive decline.
- Smoking and long-term BP appear to increase the risk of cognitive decline in elderly.
- At the population level, the most promising preventative approach would be one that considers the multicausality nature of cognitive decline.

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Conflicts of interest

None declared.

Supplementary data

Supplementary data mentioned in the text is available to subscribers in *Age and Ageing* online.

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