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Original Article

Increasing cardiovascular disease risk predicts faster cognitive decline: A Bayesian analysis of a cohort of adults in rural West Texas

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ABSTRACT

Background: Cardiovascular disease (CVD) is a major risk factor for cognitive decline and dementia. We examined whether a higher atherosclerotic cardiovascular disease (ASCVD) risk is associated with faster cognitive decline in Project FRONTIER, a rural cohort.

Methods: Participants were aged ≥40 years without baseline CVD and completed two study visits. Primary outcomes were the RBANS Total Score and its domains; secondary outcomes were Executive Interview 25, verbal fluency, Clock Drawing Test (CLOX), and Trail Making Test (TMT) A and B. Primary exposure was the 10-year ASCVD risk per AHA PREVENT equations. We fitted Bayesian mixed-effects models to estimate the interaction between time (in years) and ASCVD risk, adjusting for covariates using brms package in R.

Results: We analyzed data of 383 participants (age 57.74 ± 11.4 years; 75.5 % female; 59.8 % Hispanic; median follow-up 3.00 years, IQR: 2.67–3.64). The time×ASCVD risk interaction for RBANS Total was credibly negative (β = −1.22 points/year per 10 % higher risk, 95 % CrI −1.87 to −0.58). Strongest domain-specific effects were for attention (β = −1.25; 95 % CrI −2.14 to −0.37) and delayed memory (β = −1.36; 95 % CrI −2.16 to −0.05). CLOX suggested a credibly negative interaction (β = −0.39; 95 % CrI −0.62 to −0.16), and TMT-A showed a credibly positive interaction (β = +2.85 s/year; 95 % CrI 1.28 to 4.41).

Discussion: In this rural cohort, a higher 10-year ASCVD risk was associated with faster decline in global cognition, particularly attention and delayed memory, supporting the potential value of cardiovascular risk monitoring and modification to preserve cognitive function.

1. Background

The global population is aging at an alarming rate, with the number of individuals aged 65 and older projected to reach 1.0–1.1 billion by mid-2030 (11–13 %) and 1.6 billion (16 %) by 2050 [1]. In the United States, approximately 1 in 5 Americans (about 20–21 %) will be 65 years or older by 2030 [2]. This demographic shift brings a corresponding rise in the prevalence of age-related health conditions, including neurodegenerative diseases such as Alzheimer's disease (AD) and related dementias (ADRD). While AD remains the most common cause of dementia, vascular and mixed dementias are also major contributors, accounting for an estimated 15–25 % of cases [3]. These conditions not only profoundly impact individuals and their families but also place a substantial burden on healthcare systems worldwide.

Cardiovascular diseases (CVD) and dementia share a complex relationship [4,5]. A growing body of evidence demonstrates that major cardiovascular risk factors, such as hypertension, diabetes, dyslipidemia, and obesity, are associated with cognitive decline and dementia [6]. Pathophysiological mechanisms linking CVD and cognitive impairment include chronic microvascular disease, systemic inflammation, and the promotion of amyloid-β deposition [7]. Consequently, managing cardiovascular health has emerged as a critical strategy for preserving cognitive function in aging populations [8]. Recent AHA/ACC Hypertension Guidelines emphasize that high blood pressure is linked to increased risk of cognitive decline, and recommend an aggressive systolic BP goal of <130 mmHg for adults with hypertension

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to prevent mild cognitive impairment and dementia [9].

Rural populations face unique challenges that can exacerbate the risk of both CVD and cognitive decline. Discrepancies in access to healthcare, including a lack of specialized neurological and cardiovascular care, are well documented in rural areas [10]. These communities often experience higher rates of chronic disease, lower socioeconomic status, and greater distances to medical facilities, all of which can contribute to poorer health outcomes. Project FRONTIER (Facing Rural Obstacles to Healthcare Now Through Intervention, Education, and Research) was established to investigate the health needs of a diverse, rural population in West Texas, providing a valuable opportunity to study the interplay of these factors in a real-world setting.

Previous analyses from this cohort have highlighted the significant impact of various sociodemographic and health factors on neurocognitive function [11]. The current study extends this work by examining the longitudinal relationship between CVD risk and trajectories of cognitive function. While baseline cardiovascular risk is a known predictor, the influence of increasing risk over time is less understood. We aimed to investigate whether a higher 10-year atherosclerotic cardiovascular disease (ASCVD) risk predicts cognitive decline in a longitudinal cohort of middle-aged and older adults from Project FRONTIER. We hypothesized that increasing ASCVD risk over time would be associated with a steeper decline in neurocognitive performance. This investigation employs a Bayesian approach, which allows for more nuanced probabilistic interpretations of our findings and robust handling of complex longitudinal data.

2. Methods

2.1. Participants

Data for this study were drawn from Project FRONTIER, an ongoing, community-based longitudinal study of aging adults in rural West Texas. A detailed description of the recruitment protocol has been published previously [12]. Prior work from this study has demonstrated the comparability of the recruited cohort with the eligible population [13]. Inclusion criteria were being age $\geq$ 40 years and residing in one of the counties included in the study (Cochran, Bailey, or Parmer County, Texas). For the present analysis, we included participants who had completed at least two study visits without any history of CVD at baseline. The final sample comprised 383 participants, yielding 766 observations. All participants provided written informed consent, and the study protocol was approved by the Institutional Review Board at Texas Tech University Health Sciences Center (Legacy-L06–028-U).

2.2. Measures

The primary outcome for this study was global cognitive function, as measured by the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) Total Scale score [14]. Secondary outcomes included scores from the Executive Interview 25 (EXIT25) [15], verbal fluency (FAS) [16], Clock Drawing Test (CLOX) [17], Trail Making Test Part A and B (TMT-A and TMT-B) [18–20]. All assessments were administered by trained, bilingual research staff in the preferred language (English or Spanish) of the participant.

2.2.1. Repeatable battery for the assessment of neuropsychological status

The RBANS consists of 12 subtests that evaluate five cognitive domains: immediate memory, visuospatial/constructional abilities, language, attention, and delayed memory [14]. The RBANS is known for its strong reliability and validity and for its accuracy in assessing overall neurocognitive functioning [21]. RBANS total score and subdomains demonstrated strong internal consistency, with Cronbach's α ranging from 0.69 to 0.87 [22]. In a study involving older adults living in the community, test-retest reliability coefficients for the indexes varied from 0.58 to 0.83 [21]. The total scale often ranges from 0.75 to 0.85 [21,23]. The intraclass correlation coefficient (ICC) for the RBANS total scale was reported as around 0.77 [24].

2.2.2. Verbal fluency (FAS)

The FAS is a variant of the Controlled Oral Word Association test, a standard neuropsychological assessment technique with high sensitivity to cognitive dysfunction and dementia [25]. Verbal fluency tasks are multidimensional, as they rely on other executive functioning skills, such as processing speed, cognitive flexibility, working memory, and sustained attention [26]. Previous studies reported internal consistency (Cronbach's α) of around 0.87 across letters and trials in adult samples [27]. Furthermore, FAS showed generally good test-retest reliability (ICC = 0.64–0.90 over short intervals, varying by language and sample) [28,29], with an inter-rater reliability often reported around 0.9 [30].

2.2.3. Executive interview, 25 items (EXIT25)

EXIT25 comprises 25 tasks, including an interference task, a go/no-go task, design fluency, memory, and motor sequencing, and can therefore be more robust to task-specific confounds [15]. Therefore, EXIT25 conducts executive assessment by functioning as a more global, structured evaluation of executive control across multiple micro-tasks. The EXIT25 shows a strong correlation with other executive functioning measures, including the Wisconsin Card Sorting Task, the Trail Making Test Part B (TMT-B), Lezak's Tinker Toy Test, and the Test of Sustained Attention [15,31]. EXIT25 had moderate internal consistency (Cronbach's $\alpha = 0.66$) in a large community sample, whereas earlier work reported values of 0.87 in more impaired samples [15,32]. Inter-rater reliability is excellent (ICC = 0.96), and test-retest reliability for the total 25-item score is high (ICC = 0.86) [32].

2.2.4. Clock drawing test (CLOX)

The CLOX evaluates long-term attention, planning, visual memory, motor programming, and visuospatial/constructive skills [33,34]. CLOX 1 is an unassisted free-draw task that depends on executive control, whereas CLOX 2 emphasizes visuospatial/visuoconstructive skills. The CLOX has been validated and is reliable (Cronbach's $\alpha = 0.82$) for identifying cognitive impairment in older adults [17,35]. Wong et al. reported high test-retest reliability for both CLOX1 ($r = 0.84$) and CLOX2 ($r = 0.95$) [36]. Inter-rater reliability is also high for CLOX1 ($r = 0.84$) and CLOX2 ($r = 0.90$) [36].

2.2.5. Trail making test (TMT)

The TMT is a tool used to assess attention, visual scanning, memory, and processing speed, and it has been validated as an effective measure of cognitive function [19,37]. In both TMT-A and TMT-B, participants are tasked with connecting circles on a sheet of paper without lifting the pencil, and any mistakes are immediately corrected. Errors increase the time needed to finish the test, resulting in lower scores and indicating greater cognitive impairment. TMT-A evaluates rote memory skills, and TMT-B assesses executive function. The test-retest reliability for TMT-A ranges from 0.76 to 0.89, while for TMT-B, it ranges from 0.86 to 0.94 [37]. Furthermore, TMT is reported to be moderately internally consistent (McDonald's $\omega = 0.653$) and to have high inter-rater reliability [38]. For the Trail Making Test A and B, the inter-rater reliability was 0.996 and 0.998, respectively [39].

2.3. Cardiovascular disease risk

The primary exposure was the 10-year risk of ASCVD, calculated using the American Heart Association Predicting Risk of CVD EVENTs (PREVENT) equations separately for each visit [40]. This risk score incorporates variables such as age, sex, systolic blood pressure, cholesterol levels, smoking status, renal function, and diabetes status to estimate the 10-year likelihood of a hard ASCVD event. Systolic blood pressure was measured as the mean of three seated readings at each visit, so that the ASCVD risk score reflects standardized, longitudinally repeated blood

pressure assessment.

2.4. Covariates

Demographic and socioeconomic information was collected via self-report questionnaires. Covariates included in the models were age (standardized), sex (male vs. female), ethnicity (Hispanic vs. non-Hispanic), years of education, and annual household income. Income was treated as a categorical variable with the lowest bracket (<$20,000 per year) serving as the reference group. Diagnoses of hypertension, hyperlipidemia, and diabetes, were as follows: hypertension as defined by self-report or use of antihypertensives medications; hyperlipidemia as defined by self-report or use of cholesterol-lowering agents or total serum cholesterol greater than 220 mg/dL or low-density lipoprotein levels greater than 140 mg/dL; and diabetes mellitus as defined by self-report or history of treatment for diabetes with insulin or oral hypoglycemic agent or fasting glucose levels greater than 126 mg/dL or HBA1c of >6.5.

2.5. Statistical analysis

We analyzed the relationship between ASCVD risk and cognitive functions using a Bayesian linear mixed-effects model. Risk was treated as a time-updated covariate, and its interaction with time quantifies whether a higher ASCVD risk is associated with a faster rate of cognitive change. Analyses were conducted using available data without imputation, assuming values are missing-at-random. To assess attrition bias, we compared baseline characteristics of participants who completed the second visit with those who were lost to follow-up. A random intercept for each participant was included to account for the non-independence of repeated observations within individuals. Given the right-skewed distribution of 10-year ASCVD risk in our cohort, we rescaled risk to 10-percentage-point units (risk10 = ASCVD risk /10, expressed as a percentage) to improve the interpretability of model coefficients; accordingly, the time×risk interaction is reported per +10 % absolute increase in 10-year ASCVD risk. We also adjusted for covariates.

We specified weakly informative priors to regularize the model while allowing the data to drive the posterior estimates. Specifically, all regression coefficients were assigned a normal prior with a mean of 0 and a standard deviation of 10 (Normal(0, 10)) on the RBANS score scale. The standard deviations for the random intercept and the residual error were assigned half-Student-t priors with 3 degrees of freedom, a location of 0, and a scale of 10 (Student-t(3, 0, 10)).

All models were fitted in R (version 4.5.2) using the brms package (version 2.23.0) [41]. We ran four parallel Markov Chain Monte Carlo (MCMC) chains, with each chain consisting of 4000 iterations, including a 1000-iteration warm-up period that was discarded. Model convergence was assessed by ensuring the potential scale reduction factor ($\hat{R}$) was less than or equal to 1.01 for all parameters and by visually inspecting trace plots. We also confirmed that effective sample sizes (ESS) were sufficiently large (ESS > 1000).

Posterior distributions of the parameters were summarized using the posterior median as the point estimate, along with 95 % credible intervals (CrIs) that capture the range of plausible values. We also calculated the posterior probability of direction (pd), which quantifies the certainty that a parameter is either positive or negative. For each parameter, we reported the posterior median, posterior standard error, and CrI, which represents the range of values that contains 95 % of the posterior probability given the data and priors.

In a sensitivity analysis, we decomposed the time-updated ASCVD risk into a between-person component (mean risk across visits for each participant) and a within-person component (the deviation of each visit from that participant's mean). We entered both components, along with their time-dependent interactions, into the model to distinguish the association attributable to a participant's overall cardiovascular risk from that attributable to within-person changes in risk over time. Since the PREVENT score already incorporates age and sex, we conducted a sensitivity analysis in which the time × ASCVD-risk models for the primary outcomes (RBANS Total, Attention, and Delayed Memory) were refitted, omitting age and sex as covariates. A detailed statistical analysis is provided in the Supplementary Methods.

2.5.1. Region of practical equivalence (ROPE)

We defined the region of practical equivalence for both the primary and secondary outcomes. We established the ROPE using thresholds that identified an effect as "significant" as previously suggested by Cohen and Kruschke [42,43]. For RBANS total, a common ROPE [−0.66, +0.66] standardized units was specified around zero based on a previous analysis. This threshold corresponded to main effects and interactions (e.g., time × risk factor) on each cognitive outcome. Similarly, for immediate memory, visuospatial/constructional, language, attention, and delayed memory subdomains, ROPE values for the time × +10 % ASCVD-risk interaction were ±0.94, ±0.58, ±0.81, ±0.42, and ±0.65, respectively [44]. For secondary outcomes, the ROPE values are as follows: EXIT25: ±1.0; FAS: ±0.09; CLOX: ±0.1; TMT-A: ±20.1; and TMT-B: ±14 [45–47]. We reported the posterior probability of practical equivalence (i.e., the percentage within the ROPE).

An effect was considered credible and practically relevant when its 95 % credible interval excluded zero and only a small proportion of the posterior fell within the ROPE (indicating a non-negligible effect). When the 95 % credible interval excluded zero but most of the posterior lay within the ROPE, the effect was interpreted as directionally credible but of negligible practical magnitude. When the 95 % credible interval included zero, we concluded that there was no credible association.

3. Results

3.1. Participant characteristics

The baseline demographic and clinical characteristics of the included cohort are summarized in Table 1. The mean age of participants at baseline was 57.74 ± 11.39 years, and the sample was predominantly female (75.46 %) and Hispanic (59.79 %). The median follow-up time was 3.00 years (IQR: 2.67–3.64).

Given the high attrition rate between baseline and follow-up, we compared participants who completed a second visit with those who did not (Figure S1). The two groups were broadly similar with respect to age, ethnicity, education, income, and baseline 10-year ASCVD risk, which had identical median values across groups (4.2 %). Participants lost to follow-up were somewhat more likely to be male and had modestly lower baseline cognitive performance, including lower RBANS Total scores (83.4 vs. 85.4) and Delayed Memory scores (90.7 vs. 93.5; Table S1). Overall, attrition did not appear to be related to baseline cardiovascular risk exposure, although it was associated with slightly lower baseline cognition. This pattern is more consistent with a MAR assumption than with a strongly exposure-driven attrition mechanism.

3.2. ASCVD risk and cognitive decline

All models demonstrated excellent convergence (Figure S2–4), with all $\hat{R}$ values ≤ 1.01 and large effective sample sizes. The key parameter estimates are presented in Table 2.

3.2.1. Association of 10-year ASCVD risk with global cognition

In fully adjusted Bayesian mixed-effects models, the interaction between time and 10-year ASCVD risk on RBANS Total score was credibly negative (−1.22 points/year per 10-percentage-point higher risk, 95 % CrI: −1.87 to −0.58; pd = 99.99 %, % in ROPE = 4.5 %). To illustrate, each 10-percentage-point increase in a participant's 10-year ASCVD risk was associated with approximately one additional point of decline on the RBANS Total score per year (Fig. 1). In contrast, the main effect of baseline ASCVD risk was small and highly uncertain (1.80 points per 10

Table 1
Baseline characteristics.

Baseline Variables	Mean ± SD (n %)
Age	57.74 ± 11.39
Females (%)	289 (75.46)
Hispanic (%)	229 (59.79)
Education (years)	10.22 ± 4.46
Income:	
≤ $20 000	120 (42.11)
> $20 000	260 (57.89)
Having Insurance	247 (65.69)
Marital Status:	
Unmarried (i.e., never married, divorced, widowed, and separated)	285 (75.0)
Married	95 (25.0 %)
Follow-up time (years)	3.00 (IQR: 2.67–3.64)
10-Year ASCVD Risk at visit 1	3.55 (IQR: 1.9–7.9)
10-Year ASCVD Risk at visit 2	4.6 (IQR: 2.25–9.20)
RBANS Total Score	85.84 ± 14.34
Attention	85.45 ± 20.53
Language	91.98 ± 12.23
Visuospatial/ Constructional	81.72 ± 16.27
Immediate Memory	93.71 ± 16.34
Delayed Recall	93.57 ± 14.19
FAS Test	28.29 ± 11.45
EXIT25	6 (IQR: 3–9)
CLOX1	12 (IQR: 11–14)
CLOX2	14 (IQR: 13–14)
TMT A	45 (IQR: 36–60)
TMT B	98 (IQR: 75–140)
TC (mg/dL)	196.32 ± 40.66
HDL-C (mg/dL)	50.68 ± 14.68
Systolic BP (mm Hg)	129.59 ± 16.92
BMI (kg/m^2)	30.30 ± 6.12
HbA1c (%)	5.7 (IQR: 5.5–6.0)
eGFR (mL/min per 1.73 m^2)	89.07 (IQR: 72.04–104.36)
Antihypertensive use (%)	102 (26.63)
Statin use (%)	48 (12.53)
Smoking (%)	63 (16.45)
Diabetes (%)	91 (23.76)

RBANS-Repeatable Battery for the Assessment of Neuropsychological Status; FAS-verbal fluency; EXIT25-Exit Interview; CLOX-The Clock Drawing Test; TMT-The Trails Making Test; TC-total cholesterol; HDL-C, high-density lipoprotein cholesterol; BP- blood pressure; HbA1c-Hemoglobin A1C; eGFR-estimated glomerular filtration rate; IQR, interquartile range. Totals for some categorical variables do not sum to the full sample size due to missing data.

% increase in risk, 95 % CrI: −1.72 to 5.34; pd = 84.29 %), suggesting that cardiovascular risk primarily modified the rate of cognitive change rather than the baseline level of cognitive function. Interestingly, at very low levels of ASCVD risk, there was evidence of a slight increase in RBANS Total scores over time (0.80 points/year, 95 % CrI: 0.30 to 1.30; pd = 99.93 %), suggesting practice effects or slight improvement in this low-risk subgroup. The posterior probability of practical equivalence (proportion inside ROPE) was 4.5 %, indicating that most posterior mass lies outside the negligible range and supports a meaningful negative modification of RBANS trajectory by ASCVD risk.

3.2.2. Domain-specific RBANS outcomes

Patterns were broadly similar across RBANS domains, with 10-year ASCVD risk exerting its most apparent influence on attention and delayed memory trajectories. For RBANS Attention, the Time × +10 % ASCVD interaction was credibly negative (−1.25 points/year per 10-percentage-point higher ASCVD risk, 95 % CrI: −2.14 to −0.37; pd = 99.77 %, % in ROPE = 3.4), indicating that a 10-percentage-point higher ASCVD risk was associated with faster decline in attention. For RBANS Delayed Memory, the Time × +10 % ASCVD interaction was also credibly negative (−1.36, 95 % CrI: −2.16 to −0.05; pd = 99.55 %, % in ROPE = 2.9), indicating a faster yearly decline with higher ASCVD risk. The proportions within ROPE for attention and delayed memory were small, indicating that most of the posterior mass lies outside the

Table 2
Summary of mixed effects models.

Parameter	Median	95% CrI	pd	R̂	ESS
RBANS Total					
(Intercept)	83.96	[80.65, 87.30]	100 %	1.002	3005
Time (years)	0.8	[0.30, 1.30]	99.93 %	1.001	5273
10-year ASCVD risk	1.8	[−1.72, 5.34]	84.29 %	1.002	3473
Sex	−2.9	[−5.49, −0.27]	98.53 %	1.001	2511
Ethnicity	−5.46	[−8.55, −2.45]	99.98 %	1.002	2489
Age	−1.11	[−2.80, 0.52]	90.40 %	1.002	2906
Education	5.6	[4.07, 7.08]	100 %	1.002	2344
Income	1.32	[0.89, 1.76]	100 %	1	4541
Time x 10-year ASCVD risk	−1.22	[−1.87, −0.58]	99.99 %	1.001	5551
RBANS: immediate memory					
(Intercept)	90.5	[86.02, 95.02]	100 %	1	5101
Time (years)	0.76	[−0.03, 1.52]	96.97 %	1	7444
10-year ASCVD risk	3.56	[−1.30, 8.46]	92.03 %	1	4620
Sex	−5.15	[−8.55, −1.77]	99.85 %	1	4828
Ethnicity	−4.96	[−9.03, −0.99]	99.28 %	1	3727
Age	−2.59	[−4.81, −0.32]	98.74 %	1.001	3828
Education	2.11	[0.10, 4.04]	98.04 %	1.001	4192
Income	1.5	[0.87, 2.12]	100 %	1.001	6464
Time x 10-year ASCVD risk	−0.93	[−1.95, 0.10]	96.20 %	1	7103
RBANS: visuospatial/constructional					
(Intercept)	79.85	[75.61, 84.15]	100 %	1.001	5456
Time (years)	0.28	[−0.45, 1.02]	77.58 %	1	6604
10-year ASCVD risk	0.73	[−3.81, 5.34]	62.42 %	1.001	4694
Sex	3.69	[0.55, 6.86]	98.74 %	1	4908
Ethnicity	−5.55	[−9.23, −1.75]	99.85 %	1.001	4448
Age	−1.46	[−3.55, 0.62]	91.18 %	1	4636
Education	3.21	[1.37, 5.01]	99.95 %	1.001	4305
Income	0.91	[0.34, 1.48]	99.91 %	1	6635
Time x 10-year ASCVD risk	−0.67	[−1.64, 0.27]	92.20 %	1	6582
RBANS: language					
(Intercept)	91.05	[87.75, 94.31]	100 %	1	7491
Time (years)	−0.02	[−0.58, 0.54]	52.39 %	1	10,383
10-year ASCVD risk	−0.48	[−3.94, 3.01]	60.13 %	1	6004
Sex	−3.08	[−5.50, −0.71]	99.48 %	1.001	6190
Ethnicity	−2.27	[−5.09, 0.58]	94.35 %	1	6066
Age	0.92	[−0.69, 2.55]	87.39 %	1	5278
Education	4.49	[3.17, 5.86]	100 %	1	6286
Income	1	[0.56, 1.44]	100 %	1.001	8781
Time x 10-year ASCVD risk	−0.75	[−1.46, −0.02]	97.83 %	1	10,764
RBANS: attention					
(Intercept)	86.48	[82.22, 90.78]	100 %	1	4623
Time (years)	0.38	[−0.31, 1.04]	85.39 %	1	7328
10-year ASCVD risk	0.08	[−4.44, 4.65]	51.27 %	1.001	4758

(*continued on next page*)

Table 2 (*continued*)

Parameter	Median	95% CrI	pd	$\hat{R}$	ESS
Sex	−3.73	[−7.06, −0.42]	98.56 %	1	4166
Ethnicity	−6.01	[−9.97, −2.22]	99.92 %	1	3689
Age	−0.25	[−2.35, 1.93]	59.03 %	1	3748
Education	9.97	[8.07, 11.89]	100 %	1.001	3699
Income	1.01	[0.45, 1.59]	99.96 %	1	6590
Time x 10-year ASCVD risk	−1.25	[−2.14, −0.37]	99.77 %	1	8136
RBANS: delayed memory					
(Intercept)	90.29	[86.29, 94.20]	100 %	1.001	4143
Time (years)	1.05	[0.42, 1.66]	99.95 %	1	6709
10-year ASCVD risk	3.61	[−0.65, 7.86]	95.23 %	1.001	4044
Sex	−2.39	[−5.47, 0.68]	94.07 %	1.001	3959
Ethnicity	−1.96	[−5.50, 1.57]	85.90 %	1.002	3297
Age	−0.97	[−2.90, 0.98]	83.97 %	1.001	3677
Education	2.87	[1.12, 4.61]	99.91 %	1	3212
Income	0.95	[0.42, 1.48]	99.99 %	1.001	5190
Time x 10-year ASCVD risk	−1.36	[−2.16, −0.55]	99.95 %	1	6719
EXIT25					
(Intercept)	6.29	[5.27, 7.33]	100 %	1	10,173
Time (years)	−0.03	[−0.25, 0.20]	58.91 %	1	8387
10-year ASCVD risk	−0.4	[−1.56, 0.74]	74.63 %	1	7801
Sex	0.89	[0.20, 1.59]	99.48 %	1	12,728
Ethnicity	1.06	[0.25, 1.87]	99.43 %	1	10,503
Age	1.08	[0.61, 1.56]	100 %	1	9961
Education	−1.42	[−1.82, −1.02]	100 %	1	10,632
Income	−0.25	[−0.39, −0.11]	99.98 %	1	13,766
Time x 10-year ASCVD risk	0.16	[−0.12, 0.46]	86.42 %	1	8815
FAS					
(Intercept)	29.31	[26.54, 32.15]	100 %	1	4398
Time (years)	0.35	[−0.04, 0.73]	96.15 %	1	8609
10-year ASCVD risk	−0.9	[−3.88, 2.03]	72.73 %	1	4135
Sex	−2.07	[−4.28, 0.15]	96.66 %	1	3457
Ethnicity	−3.58	[−6.17, −0.93]	99.60 %	1.001	3021
Age	−0.66	[−2.03, 0.72]	82.63 %	1	3397
Education	4.39	[3.15, 5.66]	100 %	1.001	2800
Income	0.58	[0.21, 0.93]	99.91 %	1.001	5663
Time x 10-year ASCVD risk	−0.35	[−0.86, 0.16]	91.22 %	1	8518
CLOX					
(Intercept)	24.86	[23.92, 25.80]	100 %	1.001	7490
Time (years)	0.04	[−0.14, 0.22]	68.40 %	1	7376
10-year ASCVD risk	0.41	[−0.63, 1.43]	78.59 %	1	6168
Sex	−0.65	[−1.30, 0.01]	97.28 %	1	8138
Ethnicity	0.22	[−0.56, 1.00]	71.60 %	1	6130
Age	−0.1	[−0.54, 0.35]	66.92 %	1	6531
Education	1.11	[0.72, 1.49]	100 %	1	6264
Income	0.2	[0.07, 0.32]	99.85 %	1	9294
Time x 10-year ASCVD risk	−0.39	[−0.62, −0.16]	99.92 %	1	7592
TMT A					
(Intercept)	54.55	[47.82, 61.34]	100 %	1	6104
Time (years)	−1.9	[−3.09, −0.70]	99.88 %	1	7982
10-year ASCVD risk	−3.92	[−11.22, 3.34]	85.72 %	1	5585
Sex	4.13	[−0.95, 9.18]	94.34 %	1	5444
Ethnicity	5.15	[−0.75, 11.03]	95.67 %	1	4868
Age	8.95	[5.56, 12.28]	100 %	1	5441
Education	−12.59	[−15.52, −9.69]	100 %	1	4694
Income	−1.02	[−1.98, −0.06]	98.20 %	1	7368
Time x 10-year ASCVD risk	2.85	[1.28, 4.41]	99.98 %	1	7497
TMT B					
(Intercept)	123.66	[110.74, 136.54]	100 %	1	12,447
Time (years)	−0.12	[−2.85, 2.67]	53.22 %	1	11,137
10-year ASCVD risk	−0.89	[−13.40, 11.87]	55.25 %	1	10,480
Sex	12.94	[4.00, 21.77]	99.70 %	1	13,320
Ethnicity	11.22	[1.31, 21.01]	98.63 %	1	10,915
Age	15.86	[9.97, 21.68]	100 %	1	10,324
Education	−28.24	[−33.84, −22.67]	100 %	1	10,843
Income	−4.24	[−6.21, −2.27]	100 %	1	13,189
Time x 10-year ASCVD risk	3.25	[−0.44, 6.88]	95.83 %	1	11,312

Values are posterior medians and 95 % credible intervals (CrI) from Bayesian mixed-effects models with a random intercept for participant. Each model includes fixed effects for time since baseline (years), 10-year ASCVD risk (entered as a percentage, 0–100), sex (male vs female), ethnicity (Hispanic vs non-Hispanic), age (standardized), years of education (standardized), and annual household income (modeled as categorical variable with dividing ≤20,000/year vs. >20, 000/year). The Time × 10-year ASCVD risk term represents the additional yearly change in the cognitive outcome associated with a 10-percentage-point increase in the 10-year ASCVD risk. For RBANS indices, phonemic fluency (FAS), and clock drawing (CLOX) scores, higher values indicate better performance; for EXIT25 and Trail Making Test (TMT) times, higher values indicate worse performance (greater executive dysfunction, slower completion, and more errors). pd = posterior probability of direction (probability that the parameter is strictly positive or strictly negative); $\hat{R}$ = potential scale reduction factor (values = 1 indicate good convergence); ESS = effective sample size.

negligible range, and support a meaningful negative modification of the RBANS trajectory by ASCVD risk.

For RBANS Immediate Memory, the Time × +10 % ASCVD interaction included zero (−0.93, 95 % CrI: −1.95 to 0.10; pd = 96.20 %, % in ROPE = 51.1), indicating no credible evidence that ASCVD risk modified its rate of change. Similarly, there was no credible association of ASCVD risk with the rate of change in the Visuospatial/Constructional (−0.67, 95 % CrI: −1.64 to 0.27; pd = 92.20, % in ROPE = 48.23) or Language (−0.75, 95 % CrI: −1.46 to 0.02; pd = 97.83, % in ROPE = 57.23), domains, for which the credible intervals were compatible with no interaction.

In the decomposition sensitivity analysis, the time × between-person risk interaction for RBANS Total was credibly negative (−1.31 points/year per 10-percentage-point higher mean risk; 95 % CrI: −2.01 to −0.62; pd = 99.98 %, % in ROPE = 3.3), whereas the time × within-person risk interaction was small and not credibly different from zero

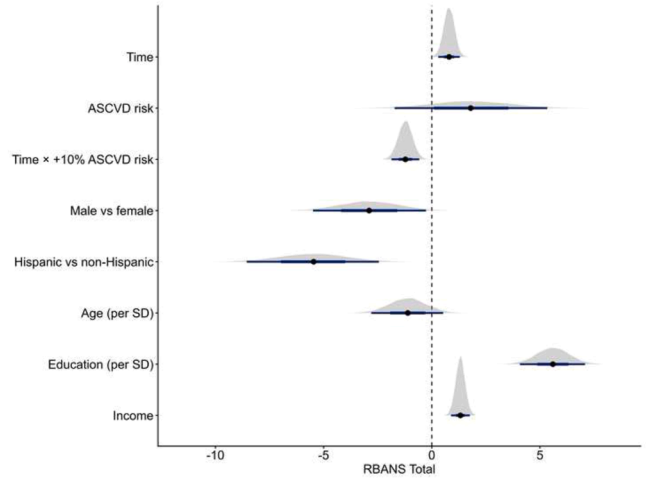

Fig. 1. Posterior estimates for predictors of RBANS Total Score. Density plots show the posterior distribution for each fixed effect from a Bayesian linear mixed-effects model. Points indicate posterior medians; thick and thin horizontal lines represent 66 % and 95 % credible intervals, respectively. The vertical dashed line indicates zero (no effect). ASCVD = atherosclerotic cardiovascular disease risk score.

(−0.20; 95 % CrI: −3.08 to 2.64; pd = 55.5 %, % in ROPE = 34.7). This indicates that the negative modification of the RBANS Total trajectory was driven primarily by a participant's overall between-person level of cardiovascular risk rather than by within-person change in risk between visits. A qualitatively similar pattern was observed for delayed memory (between-person −1.20, 95 % CrI: −2.07 to −0.34; pd = 99.69 %, % in ROPE = 10.5; within-person −2.98, 95 % CrI: −6.38 to 0.44; pd = 95.62 %, % in ROPE = 7.2), whereas for attention, both the between-person (−1.00, 95 % CrI: −2.00 to −0.04; pd = 97.97 %, % in ROPE = 12.1) and within-person (−4.47, 95 % CrI: −8.15 to −0.84; pd = 99.22 %, % in ROPE = 0.9) components were credibly negative.

When age and sex were omitted, the time × ASCVD-risk interaction for RBANS Total was −1.15 points/year (95 % CrI: −1.79 to −0.51; pd = 99.98 % in ROPE = 6.7), essentially unchanged from −1.22 points/year in the fully adjusted model. Results were likewise stable for attention (−1.19, 95 % CrI: −2.06 to −0.32; pd = 99.57 %, % in ROPE = 4.1, vs −1.25 fully adjusted) and delayed memory (−1.29, 95 % CrI: −2.09 to −0.48; pd = 99.92 %, % in ROPE = 6.0, vs −1.36 fully adjusted), indicating that the findings are not an artifact of overadjustment.

3.2.3. Executive function, fluency, and clock drawing

For executive functioning as measured by the EXIT25, the Time × +10 %ASCVD interaction was small and uncertain (0.16, 95 % CrI: −0.1201 to 0.46; pd = 86.42 %, % in ROPE = 100), indicating no clear evidence that ASCVD risk altered the trajectory of EXIT25 scores over time. Similarly, for FAS, there was no credible evidence that ASCVD risk modified longitudinal change in fluency (−0.35, 95 % CrI: −0.86 to 0.16; pd = 91.22 %, % in ROPE = 11.02). CLOX models showed weak evidence for a slightly steeper decline at higher ASCVD risk. For the CLOX total score, the Time × +10 % ASCVD interaction was −0.39 (95 % CrI: −0.62 to 0.16; pd = 99.92 %, % in ROPE = 0). Although the effect was small in magnitude, the posterior mass within the ROPE was negligible, suggesting a decline among individuals with higher ASCVD risk.

3.2.4. TMT performance

For TMT Part A, participants tended to become faster over time (−1.9 s/year, 95 % CrI: −3.09 to −0.70; pd = 99.88 %), consistent with practice-related improvement. Higher ASCVD risk attenuated these gains: the Time × ASCVD interaction was credibly positive (2.85 s/year per 10-percentage-point higher risk; 95 % CrI: 1.28 to 4.41; pd = 99.98 %; % in ROPE = 100). Thus, a 10-percentage point higher ASCVD risk was associated with approximately 2.9 s less improvement per year on TMT-A. However, the posterior probability that the interaction fell within the ROPE was approximately 100 %, indicating that the interaction magnitude is small relative to the normative-change threshold, thus unlikely to be clinically meaningful. For TMT Part B, the Time × ASCVD interaction for TMT-B was imprecise and compatible with no clear effect on change over time (−3.25, 95 % CrI: −0.44 to 6.88; pd = 95.83 %, % in ROPE = 100).

3.3. Sociodemographic covariates

Across RBANS indices, FAS, and CLOX outcomes, higher education and income were robustly associated with better cognitive performance. For example, a 1-SD higher level of education was associated with a 5.6-point higher RBANS Total score (95 % CrI: 4.07 to 7.80; pd = 100 %) and a 12.59-second faster TMT-A completion time (−12.59, 95 % CrI: −15.52 to −9.69; pd = 100 %). Higher income was also consistently associated with higher cognitive scores and fewer executive symptoms on the EXIT25.

Male sex and Hispanic ethnicity were generally associated with lower global and verbal-domain RBANS scores and worse EXIT25 performance. For RBANS Total, male sex (vs female) was associated with a −2.9-point difference (95 % CrI: −5.49 to −0.27; pd = 98.53), and Hispanic ethnicity (vs non-Hispanic) with a −5.46-point difference (95 % CrI: −8.55 to −2.45; pd = 99.98 %). However, men showed better visuospatial performance, with positive associations on the RBANS Visuospatial/Constructional index (3.69, 95 % CrI: 0.55 to 6.86; pd = 98.76 %) and CLOX components. Older age was most strongly associated with poorer performance on TMT and EXIT, while its associations with RBANS (except for the immediate memory subdomain) and fluency scores were more modest or uncertain after adjustment for other covariates.

4. Discussion

As CVD and dementias share common metabolic risk factors, vascular and mixed dementias account for ~25 % of cases. Consequently, managing cardiovascular health has emerged as a critical strategy for preserving cognitive function in aging populations. AHA PREVENT Equations were recently developed to estimate the risk of total CVD (and its subtypes) and heart failure [40]. However, the utility of the PREVENT equation in predicting cognitive decline has not been explored, particularly in a rural cohort. Hence, in this study, we attempted to explore the longitudinal effects of CVD risk on cognitive decline using a Bayesian approach in a longitudinal cohort of rural middle-aged to older adults. In this study of a rural, middle-aged to older adult cohort, we found that a higher 10-year ASCVD risk was significantly associated with a faster rate of global cognitive decline. Specifically, every 10 % increase in ASCVD risk was associated with an approximately one-point steeper annual decline in the RBANS total score. This underscores the importance of ongoing cardiovascular health management. Furthermore, this association was most pronounced for the cognitive domains of attention and delayed memory, suggesting a particular vulnerability of these functions to cardiovascular risk.

Our primary finding aligns with a large body of evidence linking cardiovascular risk factors such as hypertension, hyperlipidemia, and diabetes to cognitive impairment and dementia [4,48]. Previous studies have shown that neuropsychological performance is significantly correlated with better vascular function [49]. For instance, a study by Kaffashian et al. showed a decline in cognitive functions with increasing CVD risk scores, as measured by the Framingham Vascular Risk Score [50]. By utilizing the novel comprehensive PREVENT equations, which incorporate a range of cardiovascular risk factors to provide a global assessment of 10-year ASCVD risk, our study extends these previous findings. Furthermore, it offers a more holistic view of the impact of

cardiovascular health on cognitive aging. The observed magnitude of the effect, a one-point decline in RBANS score per year for a 10 % increase in ASCVD risk, is clinically meaningful, as even subtle changes in cognitive function can have a significant impact on an individual's quality of life and ability to perform daily activities.

The domain-specific findings of our study provide further insight into the neurocognitive profile of vascular-related cognitive decline. Prior studies have indicated that severe cerebrovascular disease can reduce cerebral perfusion and is associated with poorer global cognition, memory, psychomotor speed, executive functioning, and frontal lobe-mediated processes [51,52]. The pronounced association between ASCVD risk and accelerated decline in attention and delayed memory is consistent with the typical presentation of vascular cognitive impairment, which often involves deficits in executive function and memory retrieval [53]. In contrast, relative sparing of the visuospatial/constructional and language domains in our cohort may suggest that these cognitive functions are less susceptible to the effects of earlier stages of cardiovascular-related cognitive change. This pattern aligns with the 'subcortical-dysexecutive' profile of early vascular cognitive impairment, in which language and overlearned visuoconstructional abilities are relatively resistant to the effects of small-vessel disease [54]. Nonetheless, longer follow-up is needed to confirm whether these domains remain spared as cardiovascular burden accumulates.

Furthermore, poorer vascular risk profiles are linked to lower performance on speeded and attention-demanding measures, including TMT-A indices, as well as worse immediate and delayed memory [45,52]. The preferential vulnerability of attention and delayed memory is consistent with the known neurobiology of vascular contributions to cognitive impairment. Attention and processing speed depend on frontal-subcortical circuits and the integrity of subcortical white matter, which is especially susceptible to small-vessel disease, chronic hypoperfusion, and white-matter injury that accompany a higher cardiovascular risk burden [50,54]. Delayed memory, in turn, depends on medial-temporal and hippocampal structures that are highly sensitive to ischemia and hypoperfusion [50,55]. Thus, higher ASCVD risk may accelerate cognitive decline through vascular injury to neural systems supporting attentional control, processing efficiency, and memory consolidation/retrieval. Since the associations were not uniform across all cognitive domains, this suggests that cardiovascular risk may influence cognition in a domain-specific rather than global manner. Nevertheless, we lacked direct neurovascular characterization (e.g., vascular imaging) to identify participants with clinically significant stenosis or to quantify cerebral perfusion, which constrained our ability to test mechanistic pathways. Moreover, CVD burden in this cohort was assessed primarily through indirect indices, which may not fully capture the heterogeneous cerebrovascular pathology and its region-specific cognitive consequences.

An interesting finding of our study was a slight improvement in RBANS scores over time among individuals with very low ASCVD risk. This may be attributable to practice effects, in which repeated exposure to cognitive tests leads to improved performance [23,56]. This phenomenon is well documented in longitudinal cognitive research and highlights the importance of including a control or low-risk group to accurately interpret changes in cognitive function over time [57]. Reed et al. estimated RBANS Total practice effects of approximately 0.54 points at the first annual retest, with cumulative increases reaching 1.85 by year 2 and 4.57 by year 4 [58]. Thus, the magnitude of improvement observed in our cohort is similar to published RBANS Total practice effects, suggesting that observed longitudinal gains may partly or largely reflect retest-related improvements rather than actual cognitive gains.

We observed a sex-related pattern in which men scored lower than women on global and verbal RBANS indices and the EXIT25, but higher on visuospatial/constructional tasks and CLOX. This dissociation is consistent with the well-described female advantage in verbal learning and memory and a male advantage in visuospatial processing reported across cognitively healthy older adults [59,60]. It may also reflect sex differences in educational and occupational history within this rural cohort. These differences were accounted for in all models and therefore did not affect the association between ASCVD risk and cognitive decline.

This study has several notable strengths. Its longitudinal design enabled us to examine changes in cognitive function over time, providing stronger evidence for a temporal relationship between ASCVD risk and cognitive decline than cross-sectional studies. The use of the RBANS, a well-validated and reliable measure of global and domain-specific cognitive function, is another key strength. Furthermore, our study is one of the first to use the novel PREVENT equations to assess ASCVD risk in relation to cognitive outcomes, and our focus on a rural, predominantly Hispanic cohort addresses a significant gap in the literature, as these populations are often underrepresented in research despite a high burden of CVD.

Despite these strengths, our study also has several limitations that should be considered. First, as an observational study, we cannot establish a causal relationship between ASCVD risk and cognitive decline. Second, the median follow-up period of approximately three years is relatively short, and longer-term studies are needed to fully understand the trajectory of cognitive decline in relation to cardiovascular risk. Furthermore, with only two assessments per participant, we were able to estimate the average rate of linear change but could not characterize the shape of individual cognitive trajectories or distinguish non-linear patterns of decline. Studies with three or more repeated assessments will be needed to model cognitive trajectories more precisely. Third, our study population consisted of volunteers willing and able to participate in a longitudinal research project, which may have yielded a healthier, more motivated sample than the general population, potentially limiting the generalizability of our findings. Fourth, more than 50 % of the data from the original study were excluded due to a lack of follow-up. High participant burden may be a factor in the lack of follow-up data. Although our likelihood-based analysis is valid under a missing-at-random assumption, we cannot exclude the possibility that data were missing not at random; if participants who declined or were unable to return differed systematically in unmeasured ways, our estimates could be affected. Finally, while the RBANS is a robust screening tool, it is not a comprehensive neuropsychological battery, and a more detailed assessment of cognitive function may have revealed more subtle deficits. Although assessments were administered in the preferred language of the participant, some measures, such as verbal and executive tasks, may vary across languages, literacy levels, and acculturation. Therefore, residual measurement non-equivalence across ethnic groups cannot be excluded and may partly explain the observed ethnicity-related differences.

Our findings have important implications for both clinical practice and future research. From a clinical perspective, they underscore the critical importance of early, aggressive management of cardiovascular risk factors as a potential strategy to prevent or delay cognitive decline. The use of a global risk score, such as the PREVENT equations, could be a valuable tool for clinicians to identify individuals at high risk of cognitive impairment and motivate them to adopt healthier lifestyle behaviors. This is particularly relevant for rural and underserved populations, who may face barriers to accessing healthcare and have a higher prevalence of cardiovascular risk factors. For future research, our study highlights the need for longer-term investigations into the relationship between ASCVD risk and cognitive decline in diverse populations. Research is also needed to elucidate the mechanisms by which cardiovascular disease affects the brain, including cerebral hypoperfusion, inflammation, and white matter injury. Finally, randomized controlled trials are needed to determine whether interventions that reduce ASCVD risk can also prevent or slow the progression of cognitive decline.

5. Conclusion

In conclusion, our study provides compelling evidence that a higher 10-year ASCVD risk is a significant predictor of accelerated cognitive

decline in a rural, predominantly Hispanic cohort of middle-aged and older adults. These findings emphasize the importance of a life-course approach to cardiovascular health for the preservation of cognitive function in aging populations. Further research is needed to confirm these findings in other populations and to evaluate the effectiveness of cardiovascular risk reduction strategies for preventing cognitive decline.

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Consent statement

All participants of the Project FRONTIER study provided informed consent.

Declaration of generative AI and AI-assisted technologies

During the preparation of this work, the authors used ChatGPT (GPT-5.5, OpenAI, San Francisco, CA, USA) and Claude (Claude Opus 4.8, Anthropic, San Francisco, CA, USA) to reduce word count and improve language clarity. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content.

CRediT authorship contribution statement

Chathurika S. Dhanasekara: Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Chanaka N. Kahathuduwa:** Writing – original draft, Validation, Software, Methodology. **Volker Neugebauer:** Writing – original draft, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.tjpad.2026.100651.

Data availability

The data supporting this study were collected through Project FRONTIER and are housed at the Garrison Institute on Aging at TTUHSC. Because the data contain potentially identifying information from a small rural cohort, they are not publicly available but may be obtained from the corresponding author upon reasonable request, provided appropriate institutional and ethical approvals are in place.

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