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Temporal patterns of cognitive decline after hypertension onset among middle-aged and older adults in China

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Individuals with prevalent hypertension are at an increased risk of developing dementia and tend to exhibit lower cognitive function. However, the magnitude of cognitive change following the onset of new hypertension remains uncertain. A cohort of 7949 adults aged 45 and older without hypertension at baseline was followed prospectively for 7 years. Cognitive assessments were conducted initially (wave 1) and at least once between wave 2 (2013) and wave 4 (2018). Cognitive function was evaluated using a global cognition score, derived as a composite measure from four distinct cognitive tests. Linear mixed-effects models were employed to estimate the changes in cognitive function at the onset of hypertension (intercept change) and the subsequent rate of cognitive decline (slope change) over the follow-up period. The models accounted for pre-hypertension cognitive trajectories and participant-specific factors, with interaction terms included for antihypertensive medication, age and educational level. Of the 7949 participants, 1993 (25.07%, mean age 58.8 ± 8.84 years, 48.0% male) developed new-onset hypertension. Both groups—those without hypertension and those with new-onset hypertension—experienced annual cognitive decline during the follow-up period. The onset of hypertension was not associated with an acute decrease in global cognition or performance on the four cognitive tests. However, after the onset of hypertension, participants exhibited a statistically significant accelerated decline in global cognition (− 0.029 SD/year; 95% CI − 0.043 to − 0.015; p < 0.001), attention and calculation (− 0.022 SD/year; 95% CI − 0.040 to − 0.004; p = 0.017), and orientation (− 0.022 SD/year; 95% CI − 0.038 to − 0.005; p = 0.010). No significant changes were observed in episodic memory (− 0.009 SD/year; 95% CI − 0.028 to 0.010; p = 0.346) or visuospatial abilities (− 0.013 SD/year; 95% CI − 0.032 to 0.006; p = 0.185). Interaction analyses indicated that the use of antihypertensive medication, age, and educational level moderated the extent of global cognitive decline post-hypertension onset. The onset of new hypertension was not associated with an immediate decline in cognitive function compared to individuals without hypertension. However, it was linked to more rapid declines in global cognition, orientation, and attention and calculation abilities over time. These findings underscore the potential importance of hypertension prevention for maintaining long-term brain health.

Dementia is a common, costly, and severely debilitating condition that currently lacks effective treatments[1]. It affects approximately 57.4 million people globally, with projections suggesting this number will rise to 152.8 million by 2050[2]. Investigating the impact of vascular factors on cognitive decline may reveal potential targets for interventions to slow or prevent dementia[3]. Midlife hypertension is a significant modifiable risk factor for dementia, contributing to cognitive decline through mechanisms such as accelerated arteriosclerosis and cerebrovascular disease[4,5].

Despite established associations between hypertension and both dementia and cognitive decline[6–8], the nature of this relationship remains complex. A recent systematic review and meta-analysis of 209 prospective studies found a significant association between hypertension and increased risk of dementia and cognitive impairment[9]. However, this meta-analysis was limited by the heterogeneity among the included studies. For example, the Systolic Blood Pressure Intervention Trial (SPRINT) found that intensive blood pressure control

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did not significantly reduce dementia risk among hypertensive adults[10]. Observational studies have produced mixed findings; while some have reported a significant association between elevated blood pressure and cognitive decline[6,11–13], others have not[14–16]. These discrepancies may be attributed to variations in cognitive assessment methods, differences in follow-up durations, and diverse characteristics of the study populations.

A critical gap in the literature is the characterization of cognitive changes occurring before and after hypertension events, as well as long-term cognitive trajectories following the onset of hypertension, while accounting for individual cognitive trajectories prior to hypertension. Previous research has been limited by a lack of repeated, standardized cognitive measurements before and after hypertension events and has not adequately investigated acute cognitive changes immediately following hypertension onset. Additionally, it is important to note that most of these studies have been conducted primarily in Western populations[6,11–13]. In contrast, the relationship between blood pressure levels and cognitive decline in the Chinese population remains less well understood, despite the high prevalence of hypertension (particularly undiagnosed and/or inadequately treated hypertension) and cerebrovascular disease[17,18]. The diverse educational and economic backgrounds within the Chinese population may contribute to varying cognitive reserves, potentially leading to different patterns of cognitive trajectories.

China is experiencing a rapid demographic transition, with an increasingly aging population. The proportion of individuals aged 60 and older is expected to exceed 30% by 2030, making it one of the fastest aging countries globally[19]. This demographic shift is accompanied by a rising prevalence of chronic conditions such as hypertension, which is a leading risk factor for cognitive decline and dementia. The China Health and Retirement Longitudinal Study (CHARLS), which provides a nationally representative sample of community-dwelling middle-aged and older adults, is particularly well-suited to investigate the long-term effects of hypertension on cognitive function. This cohort represents a diverse population from various regions of China, encompassing individuals with differing socioeconomic statuses and access to healthcare. The unique characteristics of this population, such as the rapid aging process and significant regional variations in healthcare access, make it an invaluable resource for understanding the relationship between hypertension and cognitive decline in a non-Western context. By studying this cohort, we aim to provide insights that are directly applicable to China's aging population and offer critical information for public health strategies targeting the prevention and management of hypertension and related cognitive outcomes.

Method and materials

Study design, participants, and ethics

This study utilized data from the CHARLS, encompassing Wave 1 (2011) through Wave 4 (2018). CHARLS is an ongoing national survey that offers a representative sample of Chinese residents aged 45 and older[20]. Data were collected using a multi-stage stratified probability-proportional-to-size (PPS) sampling method, involving 17,705 participants from 10,257 households. The survey spans 150 counties/districts and 450 villages/urban communities across 28 provinces in China. Follow-up intervals ranged from 2 to 3 years and included data on demographics, medical history, prescription medication use, and cognitive function. CHARLS was approved by the Peking University Ethics Committee (IRB00001052-11014 and IRB00001052-11015), and all participants provided informed consent.

Of the 16,040 participants who completed the cognitive assessment at baseline, 1376 were excluded due to the following criteria: being under 45 years of age, having a history of brain injury, mental illness, stroke, or memory-related diseases such as Alzheimer's disease, brain atrophy, or Parkinson's disease. From the remaining 14,664 participants, an additional 7,170 were excluded due to a history of hypertension at baseline, missing baseline blood pressure measurements, or loss to follow-up during Waves 2 to 4 (n = 46). The detailed process of sample inclusion and exclusion is depicted in Fig. 1.

Cognitive function assessment

In each wave of the CHARLS survey, participants underwent cognitive assessments encompassing four domains: episodic memory, visuospatial ability, orientation, and attention and calculation ability. Episodic memory was assessed using a word recall test, with the total score based on the number of words correctly recalled immediately and after a 5-min delay (scoring range: 0 to 10, with each correct word counting as 0.5 points). Visuospatial ability was evaluated by having participants draw two overlapping pentagons, with successful replication scoring 1 point. Orientation was tested by asking participants to state the current date (year, month, day), day of the week, and season, with scores ranging from 0 to 5. Attention and calculation ability were measured by asking participants to subtract 7 from 100 serially up to five times, also scoring from 0 to 5. The reliability and validity of these tests have been established in previously published studies[21,22]. Z-scores were calculated for each cognitive domain using the mean and standard deviation of baseline scores, enabling direct comparisons across different domains. A z-score of 1 represents cognitive performance that is one standard deviation above the baseline mean. An overall cognitive z-score was derived by summing the individual z-scores from the four tests and then restandardizing them based on the baseline data[23].

Assessment of incidant hypertension

During the CHARLS survey, trained personnel measured blood pressure using Omron digital devices (Omron™ HEM-7200 Monitor), with three measurements taken at 45-s intervals[20]. The average of the second and third measurements was used to assess hypertension. According to the 2017 American College of Cardiology (ACC)/American Heart Association (AHA) hypertension guidelines, hypertension was defined as a systolic blood pressure above 130 mmHg, diastolic blood pressure above 80 mmHg (stage 1 hypertension), or the use of antihypertensive medication[24]. Participants were classified as currently taking antihypertensive medication if they answered "yes" to the question, "Are you currently taking any treatment to manage or control your

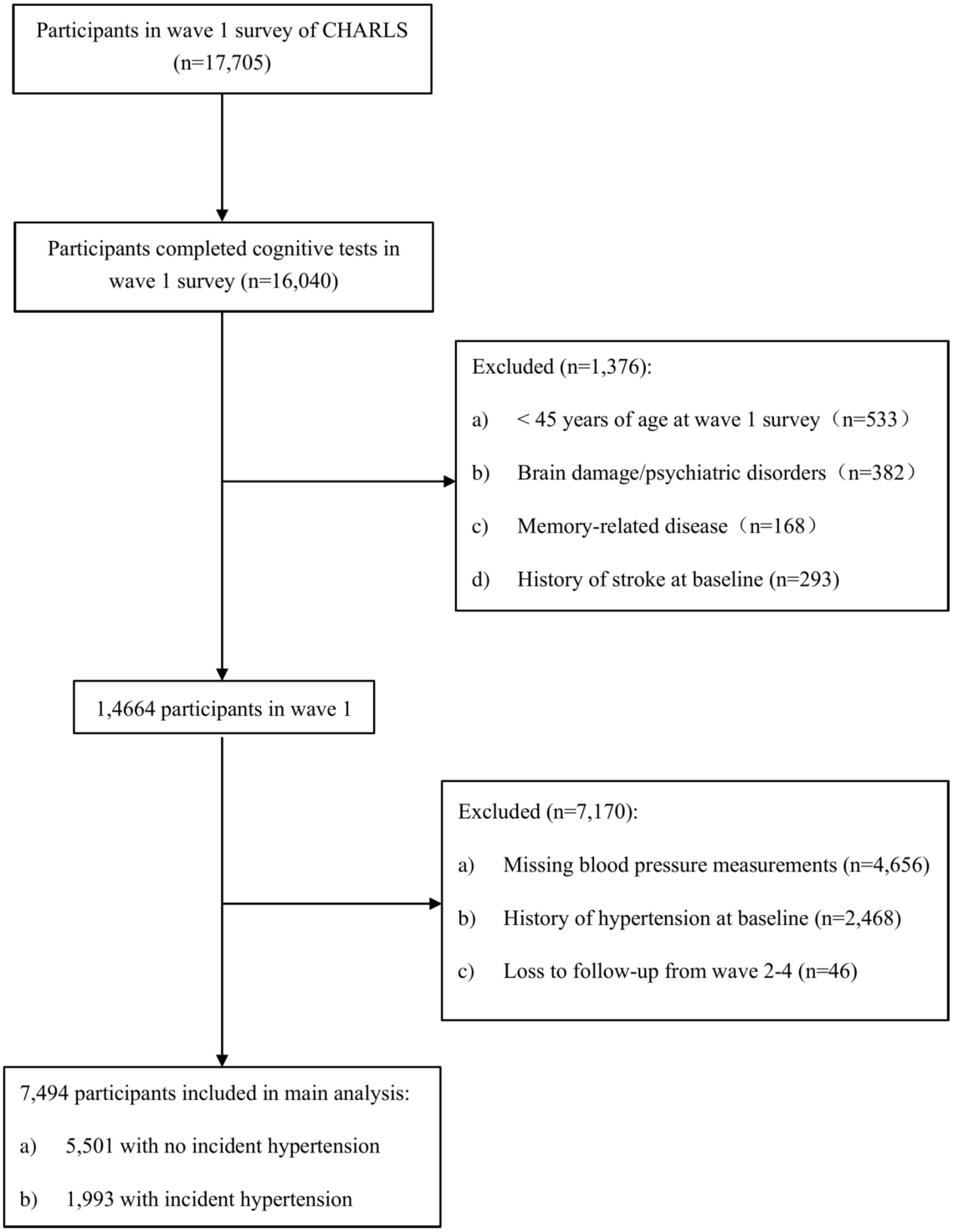

Fig. 1. Flowchart of sample selection.

hypertension?"[25]. Hypertension was also identified by self-reported physician diagnoses, with such information and medication use available for all four waves of the survey. For some participants, the onset of hypertension was determined based on their response to the question, "When were you first diagnosed with or aware of having hypertension?" For others, the onset time was estimated as the midpoint between the last survey wave in which they were not hypertensive and the first wave in which they reported having hypertension. To clarify the design of our study, we have included a clear timeline figure of the CHARLS cohort in the supplementary materials (Fig. S2). This figure visually represents the key measurement points across the four waves of data collection, highlighting when blood pressure and cognitive assessments were conducted.

Covariates

We collected data on demographic characteristics, comorbidities, lifestyle behaviors, and other health-related factors. The analysis was adjusted for baseline covariates that may be associated with hypertension or cognitive function, including age, sex, body mass index (BMI), education level, marital status, residential area, smoking status, alcohol consumption, number of instrumental activities of daily living (IADLs), diabetes, elevated total cholesterol, lung disease, myocardial infarction, cancer, and depressive symptoms. Detailed descriptions of these covariates are available in the Supplementary Methods.

Statistical analysis

Continuous data were described as mean (standard deviation, SD) or median (interquartile range, IQR) and compared using two-sample t-tests or Mann–Whitney U tests with Normality assessed via the Kolmogorov–Smirnov test. Categorical data were presented in count (percentage) and compared via Chi-square or Fisher's exact test. Linear mixed models were applied to estimate the association between new-onset hypertension and cognitive trajectories, adjusting for potential confounders. The primary independent variables in our analysis were: (1) Overall follow-up time, measured in years since baseline; (2) A time-varying binary variable representing hypertension status, which changed from 0 to 1 upon the occurrence of new-onset hypertension; (3) Time since hypertension onset, measured in years from the event's occurrence. The effect size associated with overall follow-up time represents the annual change in cognitive z-scores for all participants during the follow-up period. The effect size of the time-varying hypertension status variable captures the acute cognitive change following the onset of hypertension, defined as the immediate change in cognitive scores (intercept of the linear mixed-effects model) based on the first cognitive assessment conducted post-event and previous scores. The effect size of the post-hypertension time variable indicates the annual change in cognitive scores following new-onset hypertension, assessing whether the event is associated with an accelerated cognitive decline in subsequent years. The models included random intercepts and slopes to account for individual differences among participants.

To examine how the association between new-onset hypertension and accelerated cognitive decline varies across different covariates, such as age, gender, BMI, education level, and antihypertensive medication use, we evaluated interactions between these covariates and new-onset hypertension. Interaction terms were incorporated into the adjusted models to assess the joint effects of covariates, hypertension status, and time since hypertension onset (i.e., covariates * hypertension status * time-after-hypertension). The equations related to the linear mixed model used in this study are provided in Appendix 1. Methods.

To test the robustness of our results, we conducted several sensitivity analyses. First, we reanalyzed the association between new-onset hypertension and cognitive trajectories using raw cognitive scores to determine if the results were influenced by the use of adjusted cognitive z-scores. Second, we performed multiple imputation with 5 datasets to address missing covariate data and evaluate its impact on the findings. Details regarding the missing covariate data and imputation process are provided in the Supplementary Materials (Supplementary Fig. 1).

Data analysis was conducted from July 2023 to May 2024. All models incorporated study indices to account for heterogeneity. Statistical analyses were performed using R software (version 4.1.2; www.r-project.org), with linear mixed-effects modeling executed using the R package lme4. A two-sided P value < 0.05 was considered statistically significant.

Results

Study participants

The study sample comprised 7949 participants aged between 45 and 101 years (median [interquartile range, IQR]: 57 [50, 63]). During the 7-year follow-up period, 1,993 individuals (25.07%) developed hypertension. Baseline characteristics of participants with and without hypertension are summarized in Table 1. Those who developed new-onset hypertension were older than those who did not (median age: 58.8 years vs. 56.9 years). Compared to the control group, the hypertension group exhibited a higher number of instrumental activities of daily living (IADLs) and had greater proportions of alcohol consumption, diabetes, dyslipidemia, myocardial infarction, and depression. There was no significant difference in gender proportions between the groups. Although baseline cognitive scores in episodic memory, visuospatial ability, and orientation were lower for participants with new-onset hypertension, these differences were rendered negligible after adjusting for age, gender, and education level. The number of cognitive measurements available from Wave 1 to Wave 4 were 5501, 5,260, 5392, and 5219 for the non-hypertension group, and 1993, 1922, 1949, and 1860 for the hypertension group, respectively.

Changes in cognitive function after hypertension

At baseline, there were no significant differences in cognitive scores between participants with hypertension and those without (Table 1). Over the course of the study, cognitive function declined progressively, with an overall decline of -0.049 SD per year (-0.052 to -0.046; $p < 0.001$). Specifically, scores in all four cognitive domains decreased as follows: episodic memory by -0.026 SD per year (-0.030 to -0.021; $p < 0.001$), visuospatial ability by -0.038 SD per year (-0.043 to -0.034; $p < 0.001$), attention and calculation by -0.029 SD per year (-0.033 to -0.025; $p < 0.001$), and orientation by -0.034 SD per year (-0.038 to -0.030; $p < 0.001$). No statistically significant differences in acute cognitive decline were observed between the hypertension and control groups across overall cognitive function or the individual cognitive domains (Table 2). However, following the onset of hypertension, cognitive scores continued to decline at an accelerated rate (Figs. 2 and 3). Participants with new-onset hypertension exhibited a more rapid decline in overall cognitive scores ($\beta = -0.029$ SD per year; 95% CI, -0.043 to -0.015; $p < 0.001$; Table 2 and Fig. 2). Specifically, those with hypertension showed more pronounced declines in orientation ($\beta = -0.022$ SD per year; 95% CI, -0.038 to -0.005; $p = 0.010$) and attention

	Variables Hypertension-free group (n = 5501)	Hypertension group (n = 1993)	*P* value	*P* value*
Age	56.9 (8.46)	58.8 (8.84)	< 0.001	< 0.001
Number of IADLs	0.21 (0.53)	0.26 (0.59)	< 0.001	0.023
Cognitive test scores				
Attention and calculation	3.58 (1.61)	3.53 (1.65)	0.283	0.710
Orientation	3.84 (1.29)	3.71 (1.36)	< 0.001	0.097
Visuospatial abilities	0.66 (0.47)	0.61 (0.49)	< 0.001	0.188
Episodic memory	3.70 (1.66)	3.55 (1.66)	0.002	0.674
Male participants	2585 (47.0%)	957 (48.0%)	0.447	0.290
Education			< 0.001	0.035
Illiterate	2409 (43.8%)	978 (49.1%)		
Primary school	1198 (21.8%)	444 (22.3%)		
Middle school	1228 (22.3%)	384 (19.3%)		
High school and above	666 (12.1%)	187 (9.38%)		
Marital status			0.002	0.096
Other status	736 (13.4%)	325 (16.3%)		
Married	4765 (86.6%)	1668 (83.7%)		
Residential area			0.075	0.350
Urban	1909 (34.7%)	647 (32.5%)		
Rural	3592 (65.3%)	1346 (67.5%)		
Heart attack	381 (6.96%)	193 (9.71%)	< 0.001	< 0.001
Diabetes	171 (3.13%)	91 (4.60%)	0.003	0.002
Cancer	39 (0.71%)	12 (0.60%)	0.735	0.561
Lung diseases	437 (7.97%)	185 (9.31%)	0.072	0.289
High total cholesterol	265 (4.88%)	159 (8.09%)	< 0.001	< 0.001
Current drinking	2079 (37.8%)	834 (41.9%)	0.002	0.001
Current smoking	2137 (38.8%)	803 (40.3%)	0.27	0.719
Depression	1359 (24.7%)	559 (28.1%)	0.004	0.047

Table 1. Baseline participant characteristics by incident hypertension. Data are represented as mean ± standard deviation (SD) or n (%). *IADLs* Instrumental activities of daily living score. *Calculated using generalized linear models for continuous covariates and logistic regression for categorical covariates after adjustment for baseline age, sex and education level.

Cognitive Domains	Cognitive change over time[a]	Acute change after incident hypertension[b]	Changes in slope after incident hypertension[c]
	β (95% CI)	β (95% CI)	β (95% CI)
Global cognition	**− 0.049 (− 0.052 to − 0.046)**	− 0.004 (− 0.45 to 0.038)	**− 0.029 (− 0.043 to − 0.015)**
Episodic memory	**− 0.026 (− 0.030 to − 0.021)**	− 0.031 (− 0.087 to 0.026)	− 0.009 (− 0.028 to 0.010)
Visuospatial abilities	**− 0.038 (− 0.043 to − 0.034)**	− 0.029 (− 0.086 to 0.027)	− 0.013 (− 0.032 to 0.006)
Attention and calculation	**− 0.029 (− 0.033 to − 0.025)**	0.007 (− 0.046 to 0.059)	**− 0.022 (− 0.04 to − 0.004)**
Orientation	**− 0.034 (− 0.038 to − 0.030)**	0.03 (− 0.02 to 0.08)	**− 0.022 (− 0.038 to − 0.005)**

Table 2. New-onset hypertension and change in cognitive performance over time. The table includes results from mixed linear regression models with subject-specific random intercepts and slopes. These models adjust for several covariates: age, gender, body mass index (BMI), instrumental activities of daily living (IADLs) score, education level, residential area (rural or urban), marital status, smoking, alcohol use, hyperlipidemia, cancer, diabetes, myocardial infarction, lung disease, depressive symptoms, time (years), and the time-varying hypertension variable (all subjects were event-free at baseline). Additionally, the models include a time variable representing the years since the hypertension onset. The effect sizes presented in the table indicate the following: [a] Annual Change in Cognitive Scores: This effect size shows the yearly change in cognitive scores for each of the four tests. It represents the general trend of cognitive decline over time for all participants, regardless of hypertension status. [b] Acute Change in Cognitive Scores Post-Hypertension: This effect size reflects the immediate change in cognitive scores after hypertension onset, compared to before the event. It highlights the short-term impact of hypertension on cognitive function. [c] Annual Change in Cognitive Scores Post-Hypertension: This effect size shows the yearly change in cognitive scores for each of the four tests after hypertension onset. It indicates the long-term trend of cognitive decline for participants who have experienced hypertension, assessing whether the cognitive decline accelerates after the event. Bold represents significant result at $p < 0.05$.

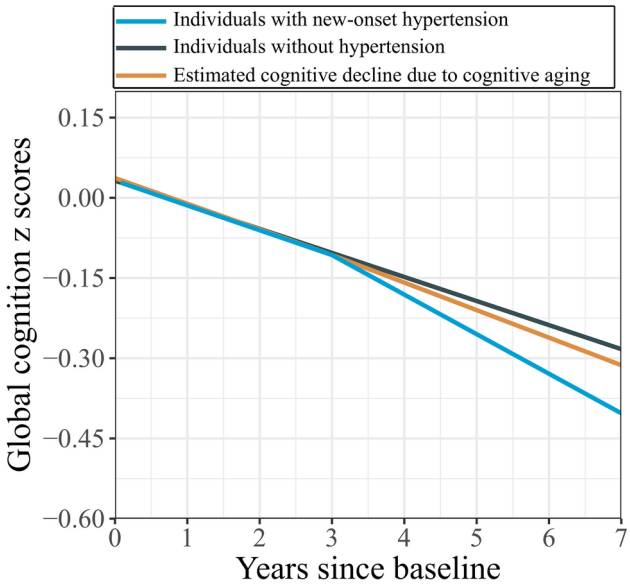

Fig. 2. Predicted changes in global cognition z-scores over time. The predicted values were derived from the results of the mixed-effects model regression (Table 2), which adjusted for random intercepts and slopes for baseline age, gender, body mass index (BMI), instrumental activities of daily living (IADLs) score, education level, residential area (rural or urban), marital status, smoking, alcohol use, hyperlipidemia, cancer, diabetes, myocardial infarction, lung disease, depressive symptoms, time (years), the time-varying hypertension variable (all subjects were hypertension-free at baseline), and the time variable representing the time (years) after new-onset hypertension. The predicted cognitive scores are calculated for a 60-year-old woman with the following characteristics: she completed primary education, resides in a rural area, is married, and does not currently smoke or drink. She does not have diabetes, dyslipidemia, lung diseases, heart attack, cancer, or depression. Her IADL score is 0. She developed hypertension at the end of the third year.

and calculation (β = − 0.022 SD per year; 95% CI, − 0.040 to − 0.004; p = 0.017) compared to the control group. In contrast, there were no significant differences in the rate of decline in episodic memory (β = − 0.009 SD per year; 95% CI, -0.028 to 0.010; p = 0.346) or visuospatial ability (β = − 0.013 SD per year; 95% CI, − 0.032 to 0.006; p = 0.185) between the groups. Figures 2 and 3 illustrate the estimated cognitive trajectories for a representative participant based on the parameters from the multivariable models in Table 2.

Risk factors for cognitive decline

Individuals not using antihypertensive medication exhibited a more pronounced decline in overall cognitive function after the onset of hypertension (β = −0.027 SD per year; 95% CI, −0.048 to −0.005; p = 0.014), as well as in attention and calculation (β = −0.040 SD per year; 95% CI, − 0.078 to − 0.003; p = 0.036) and orientation (β = −0.036 SD per year; 95% CI, −0.061 to −0.011; p = 0.005). In contrast, participants using antihypertensive medication did not experience significant cognitive deterioration in overall scores or across the four cognitive domains post-hypertension (Table 3). Age was found to significantly modify the effect of hypertension on cognitive decline (p for interaction < 0.001, Fig. 4). Older individuals (aged ≥ 60 years) experienced a more rapid decline in overall cognitive function post-hypertension, with a rate of −0.045 SD per year (95% CI, −0.073 to −0.018), compared to −0.020 SD per year (95% CI, −0.036 to −0.004) in middle-aged individuals (aged 45–60 years). A history of myocardial infarction did not correlate with a statistically significant acceleration in cognitive decline following hypertension (β = −0.019 SD per year; 95% CI, −0.060 to 0.022), whereas individuals without such a history showed a more pronounced decline in overall cognitive scores post-hypertension (β = −0.031 SD per year; 95% CI, −0.046 to −0.017; p for interaction < 0.001). Additionally, interactions between hypertension and lower education level (below middle school), smoking, and rural residence were significant (Fig. 4).

Sensitivity analysis

To assess the robustness of our findings related to adjusted cognitive z-scores, we reanalyzed the data using raw cognitive scores without adjustments. This reanalysis revealed that individuals still exhibited a significantly accelerated decline in attention and calculation (−0.036 SD per year; 95% CI, −0.065 to −0.006) and orientation (−0.028 SD per year; 95% CI, −0.050 to −0.007) following the onset of hypertension. However, no significant changes were observed in episodic memory or visuospatial ability (Supplementary Table 1). Additionally, to examine the impact of missing baseline covariate data (Supplementary Fig. 1) on our results, we performed multiple imputations. The results from this analysis were consistent with the original findings, demonstrating an accelerated decline in overall cognitive function, attention and calculation, and orientation post-hypertension (Supplementary Table 2).

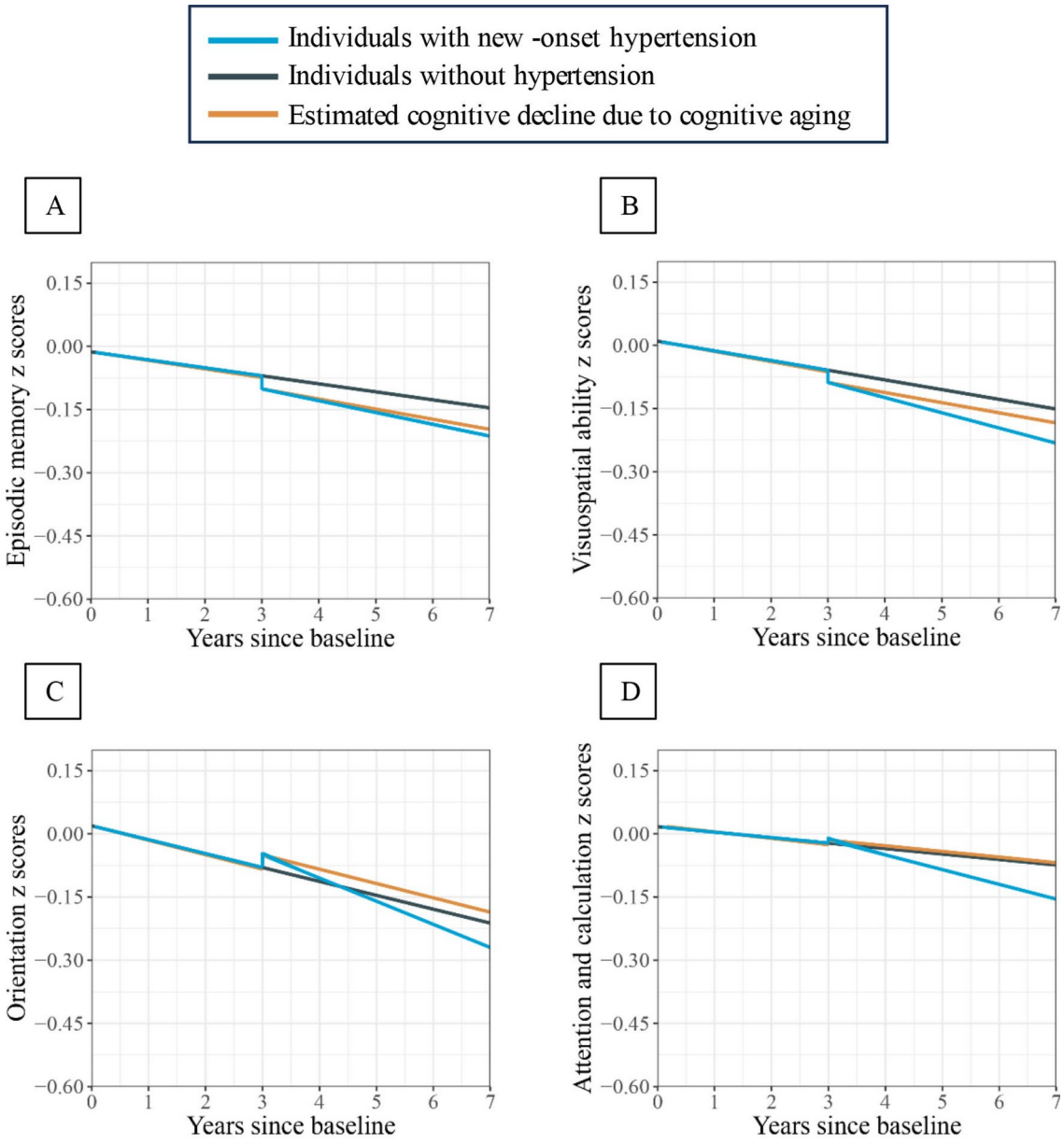

Fig. 3. Estimated changes in z-scores of different cognitive tests over time. The predicted values were derived from the results of the mixed-effects model regression (Table 2), which adjusted for random intercepts and slopes for baseline age, gender, body mass index (BMI), instrumental activities of daily living (IADLs) score, education level, residential area (rural or urban), marital status, smoking, alcohol use, hyperlipidemia, cancer, diabetes, myocardial infarction, lung disease, depressive symptoms, time (years), the time-varying hypertension variable (all subjects were hypertension-free at baseline), and the time variable representing the time (years) after new-onset hypertension. The predicted cognitive scores are calculated for a 60-year-old woman with the following characteristics: she completed primary education, resides in a rural area, is married, and does not currently smoke or drink. She does not have diabetes, dyslipidemia, lung diseases, heart attack, cancer, or depression. Her IADL score is 0. She developed hypertension at the end of the third year.

Discussion

In this extensive prospective cohort study, which included predominantly Chinese individuals aged 45 and older with no history of hypertension or significant cognitive impairment at baseline, new-onset hypertension was associated with a long-term decline in global cognition, as well as in orientation, attention, and calculation abilities. Although we did not observe a significant acute decline in cognitive function at the time of hypertension onset, there was an accelerated decline in these cognitive domains several years after the onset of hypertension. In contrast, the rate of decline in episodic memory and visuospatial abilities did not show a significant increase following hypertension onset. Notably, among individuals receiving antihypertensive medication, there was neither an acute decline in cognitive function nor an accelerated decline in subsequent years post-hypertension.

Cognitive Domains Across Subgroups	Cognitive change over time	Acute change after incident hypertension	Changes in slope after incident hypertension
	β (95% CI)	β (95% CI)	β (95% CI)
Not taking anti – HTN			
Global cognition	**−0.049 (−0.052 to −0.045)**	−0.008 (−0.062 to 0.047)	**−0.027 (−0.048 to −0.005)**
Episodic memory	**−0.025 (−0.030 to −0.021)**	−0.004 (−0.080 to 0.072)	−0.015 (−0.044 to 0.015)
Visuospatial abilities	**−0.039 (−0.043 to −0.034)**	−0.0168 (−0.092 to 0.059)	−0.008 (−0.038 to 0.022)
Attention and calculation	**−0.029 (−0.033 to −0.025)**	−0.052 (−0.123 to 0.018)	**−0.040 (−0.078 to −0.003)**
Orientation	**−0.034 (−0.038 to −0.030)**	0.040 (−0.025 to 0.105)	**−0.036 (−0.061 to −0.011)**
Taking anti – HTN			
Global cognition	**−0.071 (−0.096 to −0.047)**	0.048 (−0.032 to 0.128)	−0.008 (−0.038 to 0.023)
Episodic memory	**−0.060 (−0.091 to −0.029)**	−0.047 (−0.151 to 0.056)	0.020 (−0.019 to 0.059)
Visuospatial abilities	**−0.056 (−0.086 to −0.026)**	0.005 (−0.097 to 0.106)	0.003 (−0.035 to 0.041)
Attention and calculation	**−0.025 (−0.055 to 0.005)**	0.092 (−0.005 to 0.190)	−0.009 (−0.037 to 0.020)
Orientation	**−0.053 (−0.083 to −0.023)**	0.074 (−0.027 to 0.176)	0.007 (−0.030 to 0.044)

Table 3. Changes in cognitive z-scores after hypertension according to age at hypertension onset[a]. [a] Adjusted for baseline age, gender, body mass index (BMI), instrumental activities of daily living (IADLs) score, education level, residential area (rural or urban), marital status, smoking, alcohol use, hyperlipidemia, cancer, diabetes, myocardial infarction, lung disease, depressive symptoms, time (years), the time-varying hypertension variable (all subjects were hypertension-free at baseline), and the time variable representing the time (years) after new-onset hypertension. Bold represents significant result at $p < 0.05$.

These results were robust across various risk factors, indicating that effective management of hypertension may mitigate long-term cognitive decline.

The cognitive trajectories associated with new-onset hypertension remain underexplored, particularly within Asian populations. While several longitudinal studies have investigated cognitive function at multiple time points in individuals who developed hypertension during follow-up, few have specifically examined how cognitive trends post-hypertension onset compare to pre-hypertension trends. Our study adds to the existing literature on dementia and cognitive decline related to hypertension[6–8], revealing that cognitive decline following new-onset hypertension is not abrupt but rather accelerates over the subsequent years. This decline appears to be influenced by factors such as age, history of myocardial infarction, education level, and residential area. For instance, the Baltimore Longitudinal Study of Aging noted that elevated systolic blood pressure was associated with poorer initial cognitive performance but a slower decline in individuals aged 60, whereas those aged 80 and older experienced a faster cognitive decline with higher systolic pressure. This study also highlighted nonlinear effects of systolic and diastolic blood pressure, and complex interactions with age, medication, education, and alcohol intake, underscoring the intricate relationship between blood pressure and cognitive decline[26]. Our findings suggest that the cognitive impact of hypertension intensifies with longer exposure. A previous study, which tracked mean systolic and diastolic blood pressure over 19 years, found these measurements to be more predictive of cognitive decline than baseline blood pressure[27]. However, this and similar studies did not specifically address new-onset hypertension[28]. We observed that cognitive decline related to new-onset hypertension was subtle, predominantly manifesting during the 7-year follow-up period, with minimal immediate changes post-onset. This supports the concept that hypertension contributes to a gradual and progressive decline in brain function, emphasizing the potential for early intervention to mitigate long-term effects.

The Maastricht Aging Study (MAAS), a prospective cohort study examining brain aging, tracked cognitive function among individuals aged 25 to 84 years with prevalent hypertension and those who developed hypertension during follow-up (at baseline, year 6, and year 12). This study found that participants with new-onset hypertension experienced more rapid declines in memory and information processing speed, particularly among those with poorly controlled blood pressure and middle-aged to older adults[29]. In contrast, our study revealed distinct patterns of cognitive decline. We did not observe an accelerated decline in episodic memory and visuospatial ability following hypertension onset, which contrasts with findings from the MAAS. The reasons for these discrepancies remain unclear and warrant further investigation. Future neuroimaging studies may provide insights into the underlying mechanisms that differentially affect various cognitive domains. Our research highlights a steeper decline in orientation, attention, and calculation abilities among individuals with new-onset hypertension, thereby offering a more nuanced understanding of cognitive changes. The lack of significant decline in episodic memory and visuospatial ability in our study may be attributed to differences in disease duration and follow-up periods. These findings underscore the importance of monitoring cognitive impairment in hypertensive patients, particularly soon after diagnosis, to better understand and manage the progression of cognitive decline.

Our analysis reveals no significant acceleration in cognitive decline among individuals receiving antihypertensive medication. In contrast, untreated hypertensive patients exhibited a more pronounced and widespread deterioration in cognitive function. This finding is consistent with the observation that hypertensive individuals often present with greater white matter lesions, as noted in prior research[30]. These results suggest that antihypertensive treatment may confer protective benefits for brain health and highlight the importance of rigorous blood pressure management. However, our data do not address whether elevated blood pressure in

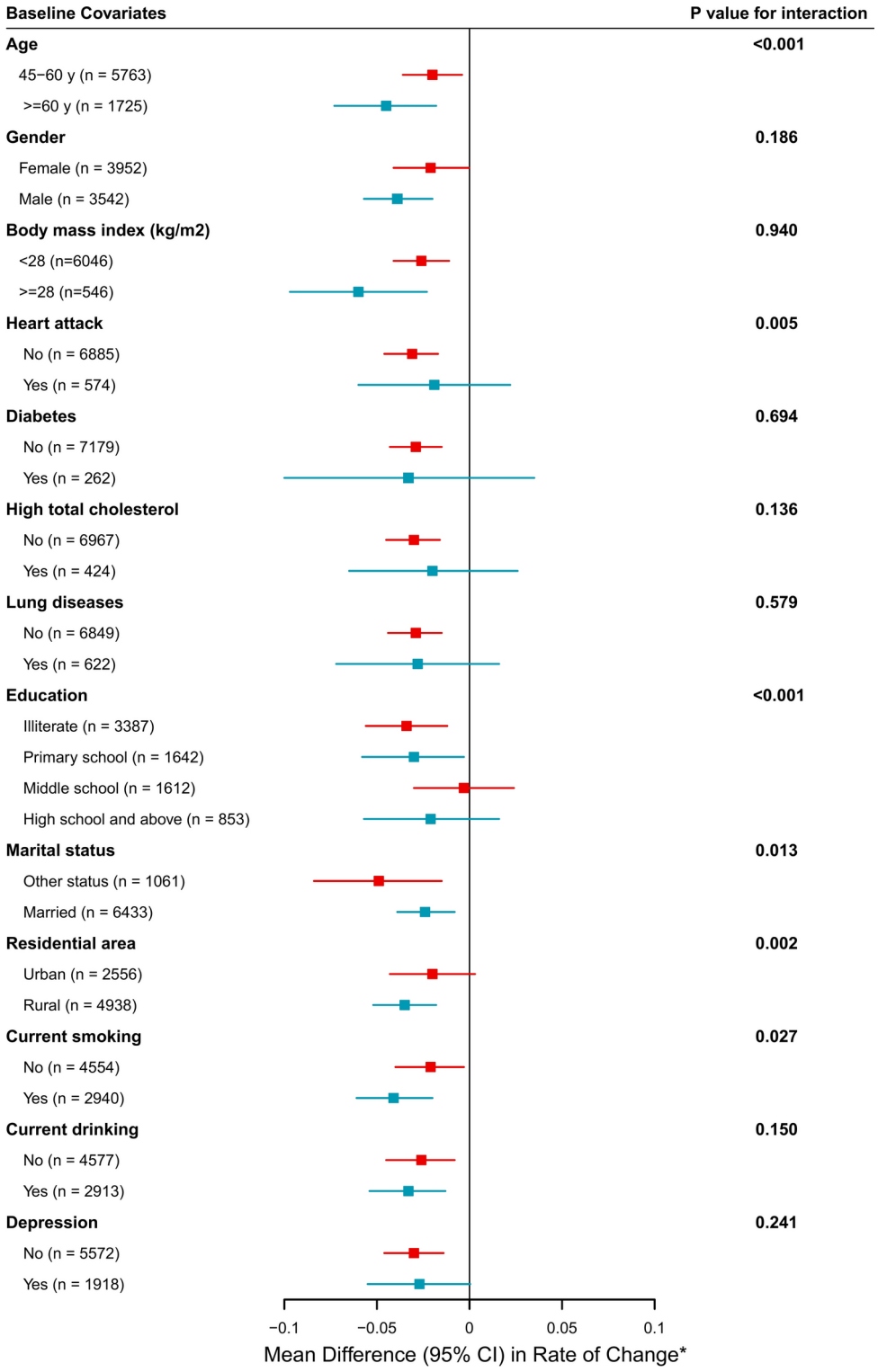

Fig. 4. Post-hypertension annual decline in global cognitive z-scores after hypertension onset, according to subgroups defined by covariates. *After adjusting for baseline age, gender, body mass index (BMI), instrumental activities of daily living (IADLs) score, education level, residential area (rural or urban), marital status, smoking, alcohol use, hyperlipidemia, cancer, diabetes, myocardial infarction, lung disease, depressive symptoms, time (years), the time-varying hypertension variable (all subjects were hypertension-free at baseline), and the time variable representing the time (years) after new-onset hypertension, except where an adjusting variable was itself being tested.

treated individuals was attributable to poor medication adherence. Furthermore, there may be an indication bias, as those on antihypertensive therapy could be in more advanced stages of disease or have additional vascular comorbidities. Consequently, suboptimal hypertension control in this group might reflect a higher overall vascular burden.

The absence of significant short-term cognitive changes across the study population indicates that cognitive impairments are unlikely to be attributable to acute illness or delirium, but rather represent a gradual decline. This observation underscores the role of common vascular risk factors—such as new-onset hypertension, myocardial infarction, and vascular dementia—in shaping cognitive trajectories over time[31–33]. While we have meticulously accounted for established vascular risk factors, it is important to recognize that subclinical disease or pre-disease states may also contribute to cognitive decline. Further investigation into these early disease states could provide additional insights into the mechanisms underlying gradual cognitive impairment.

Our study revealed that age acts as an effect modifier in the association between new-onset hypertension and accelerated cognitive decline, with older adults (age ≥ 60) exhibiting a more pronounced decline in global cognition compared to their middle-aged counterparts. This finding aligns with existing research[34], which suggests that cognitive decline in older individuals is more susceptible to environmental influences. Consequently, mitigating cognitive decline or dementia should be a focal point of preventive strategies for older adults with hypertension. Additionally, our analysis identified several socioeconomic and lifestyle factors, including educational level, marital status, and residential area (urban vs. rural), as significant modifiers of the relationship between hypertension onset and cognitive decline. These factors may reflect underlying complexities beyond biological mechanisms, such as variations in cognitive assessment methods, which warrant further investigation.

New-onset hypertension may influence cognitive trajectories through several mechanisms. Chronic hypertension exerts increased pressure on arterial walls, potentially leading to the development of atherosclerosis[35]. Over time, this can impair cerebral perfusion, resulting in microinfarctions and other manifestations of small vessel disease within the brain[36]. The association between elevated blood pressure and white matter lesions is well-documented[36,37], particularly in individuals with midlife or poorly controlled hypertension[38,39].

This study has several notable strengths. It is among the largest investigations to examine cognitive trajectories before and after new-onset hypertension within a Chinese population. The extensive sample size and repeated measurements provided a robust dataset, enabling precise and reliable assessments of cognitive changes over time. Furthermore, our analysis offers valuable insights by including subgroup analyses of younger participants, which extends previous research in this area.

Nevertheless, several limitations must be acknowledged. First, the follow-up period in CHARLS is relatively brief, capturing cognitive changes shortly after hypertension onset. Since hypertension is a chronic condition, the long-term cognitive effects may not be fully reflected in our findings. Additionally, the cognitive assessment tools used were limited, and the hypertension diagnosis for some participants might lack precision. The predominance of individuals from rural areas in the study population may also restrict the generalizability of the results to other populations or to long-term outcomes beyond the initial follow-up period. Second, the absence of the Mini-Mental State Examination (MMSE) in the first through third waves of CHARLS prevented us from defining dementia or mild cognitive impairment (MCI) using established cognitive score cutoffs. Third, despite adjusting for numerous confounders, there may be additional unmeasured variables—such as apolipoprotein E (ApoE) genotype and air pollution—that could influence the results. While the frequency of the ApoEε4 allele in the Chinese population is approximately 7%[40], its impact on our findings is likely minimal. Fourth, some hypertension cases may have been misdiagnosed, potentially representing conditions like white coat hypertension, which is more prevalent among women and younger individuals when blood pressure is measured by a physician rather than a technician. Fifth, one limitation of this study is the challenge of accurately capturing the onset of hypertension and the exact temporal association with cognitive decline. The development of hypertension is a gradual and insidious process, and due to the relatively large time intervals between measurements and cognitive assessments in the CHARLS cohort, we were unable to precisely identify the moment of hypertension onset for each participant. As a result, while our study provides valuable insights into the general association between hypertension onset and subsequent cognitive decline, it is important to acknowledge that the precise temporal dynamics of this relationship remain difficult to assess. These limitations are inherent in the design of longitudinal cohort studies with sparse measurement intervals, and future studies with more frequent assessments may provide a clearer understanding of the onset and progression of hypertension in relation to cognitive decline. Lastly, being an observational study, our research can identify associations but cannot establish causality.

Conclusion

New-onset hypertension is not associated with immediate cognitive decline; however, it is linked to an accelerated rate of cognitive deterioration over time. This underscores the importance of vigilant long-term monitoring of cognitive function in individuals with hypertension. Regular assessment of cognitive health in patients who develop hypertension is essential, particularly in the years following the onset of the condition. Additionally, effective management of blood pressure may play a crucial role in mitigating the rate of cognitive decline.

Data availability

The data utilized in this manuscript were derived from the China Health and Retirement Longitudinal Study (CHARLS). We obtained permission for data access through the CHARLS website (http://charls.pku.edu.cn). The principal investigators of CHARLS are Prof. Yaohui Zhao (National School of Development, Peking University), John Strauss (University of Southern California), and Gonghuan Yang (Chinese Center for Disease Control and Prevention).

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Author contributions
Shouqiang Zhu contributed to drafting the article. Xiaoping Gu, Tianjiao Xia and Shouqiang Zhu contributed to the conception and design of the study. Shouqiang Zhu and Jinhua Bo contributed to the analysis and interpretation of data. Xiaoping Gu and Tianjiao Xia contributed to reviewing the final manuscript.

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Declarations

Competing interests
The authors declare no competing interests.

Ethics declaration
Ethical approval for all the CHARLS waves was granted by the Institutional Review Board (IRB) at Peking University. The IRB approval number for the main household survey, including anthropometrics, is IRB00001052-11015. All methods in this study were performed in accordance with the guidelines of the Declaration of Helsinki. Clinical trial number: not applicable.

Informed consent
During the fieldwork, each respondent who agreed to participate in the survey signed two copies of an informed consent form; one copy was retained at the CHARLS office, where it was also scanned and saved in PDF format. For participants who were illiterate or otherwise vulnerable, informed consent was obtained from a parent and/or legal guardian.

Additional information
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