

Supplement

Appendix 1. Methods

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Covariates

Educational attainment was categorized into four levels: illiterate, primary school, middle school, and high school or above. Marital status was dichotomized as married versus other. Diabetes was defined based on a self-reported physician's diagnosis, use of antidiabetic medication, or hemoglobin A1c (HbA1c) level of 6.5% or higher. High total cholesterol was classified according to self-reported diagnosis, use of lipid-lowering medications, or a serum total cholesterol concentration of 240 mg/dL or greater. Depressive symptoms were assessed using the 10-item Centre for Epidemiologic Studies Depression Scale Short Form, with a score of 10 or higher (on a scale of 0 to 30) indicating depression.

Diagnosis time

In the CHARLS study, the diagnosis timing was recorded only to the year, rather than to the month, for most participants. By default, we set the measurement time for cognitive function at the midpoint of the year and designated the time of incident hypertension as the beginning of the year. We then reviewed each hypertension participant's questionnaire to determine whether the hypertension diagnosis occurred after the interview. If so, we adjusted the timing of the hypertension event to the end of the year. This approach aimed to enhance the accuracy of our analysis.

Equation 1: Linear Mixed Model (Basic Form)

$$Y_{it} = \beta_0 + \beta_1 * Time_{it} + \beta_2 * Hypertension_{it} + \beta_3 * Time_{since_hypertension_it} + u_i + \varepsilon_{it}$$

Where:

Y_{it} : Cognitive score (or z-score) for participant i at time t .

$Time_{it}$: Time (in years) since baseline for participant i .

$Hypertension_{it}$: Binary variable (0 = no hypertension, 1 = hypertension) indicating whether hypertension has occurred.

$Time_{since_hypertension_it}$: Time (in years) since hypertension onset for participant i .

u_i : Random intercept for participant i , accounting for individual differences.

ε_{it} : Error term for participant i at time t .

Equation 2: Model with Interaction for Covariates

$$Y_{it} = \beta_0 + \beta_1 * Time_{it} + \beta_2 * Hypertension_{it} + \beta_3 * Time_since_hypertension_{it} + \beta_4 * Covariates_{it} + u_i + \varepsilon_{it}$$

Where:

Covariates_{it}: Time-varying covariates (e.g., age, gender, BMI, education).

This model also allows interaction between Hypertension_{it} and Covariates_{it} to examine if the effect of hypertension on cognitive decline is modified by these factors.

Table S1. Sensitivity Analysis: Relationship Between New-Onset Hypertension and Cognitive Changes Over Time Using Raw Cognitive Scores

	Cognitive change over time	Acute change after incident hypertension	Changes in slope after incident hypertension
	β (95% CI)	β (95% CI)	β (95% CI)
Episodic memory	-0.043 (-0.050 to -0.035)	-0.064 (-0.159 to 0.030)	-0.015 (-0.047 to 0.016)
Visuospatial abilities	-0.018 (-0.021 to -0.016)	-0.014 (-0.041 to 0.013)	-0.006 (-0.016 to 0.003)
Attention and calculation	-0.047 (-0.054 to -0.041)	0.011 (-0.074 to 0.096)	-0.036 (-0.065 to - 0.006)
Orientation	-0.044 (-0.050 to -0.039)	0.040 (-0.026 to 0.105)	-0.028 (-0.050 to - 0.007)

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.

Table S2. Sensitivity Analysis: Multiple Imputation for Missing Covariates and Relationship Between New-Onset Hypertension and Cognitive Changes Over Time

	Cognitive change over time	Acute change after incident hypertension	Changes in slope after incident hypertension
	β (95% CI)	β (95% CI)	β (95% CI)
Global cognition	-0.047 (-0.050 to -0.044)	0.003 (-0.036 to 0.041)	-0.029 (-0.042 to -0.016)
Episodic memory	-0.024 (-0.029 to -0.020)	-0.028 (-0.081 to 0.025)	-0.015 (-0.032 to 0.003)
Visuospatial abilities	-0.035 (-0.040 to -0.031)	-0.018 (-0.070 to 0.035)	-0.015 (-0.033 to 0.003)
Attention and calculation	-0.028 (-0.032 to -0.025)	0.014 (-0.035 to 0.062)	-0.021 (-0.038 to -0.005)
Orientation	-0.033 (-0.037 to -0.029)	0.022 (-0.025 to 0.068)	-0.021 (-0.036 to -0.006)

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.

Figure S1. Missingness of Covariates

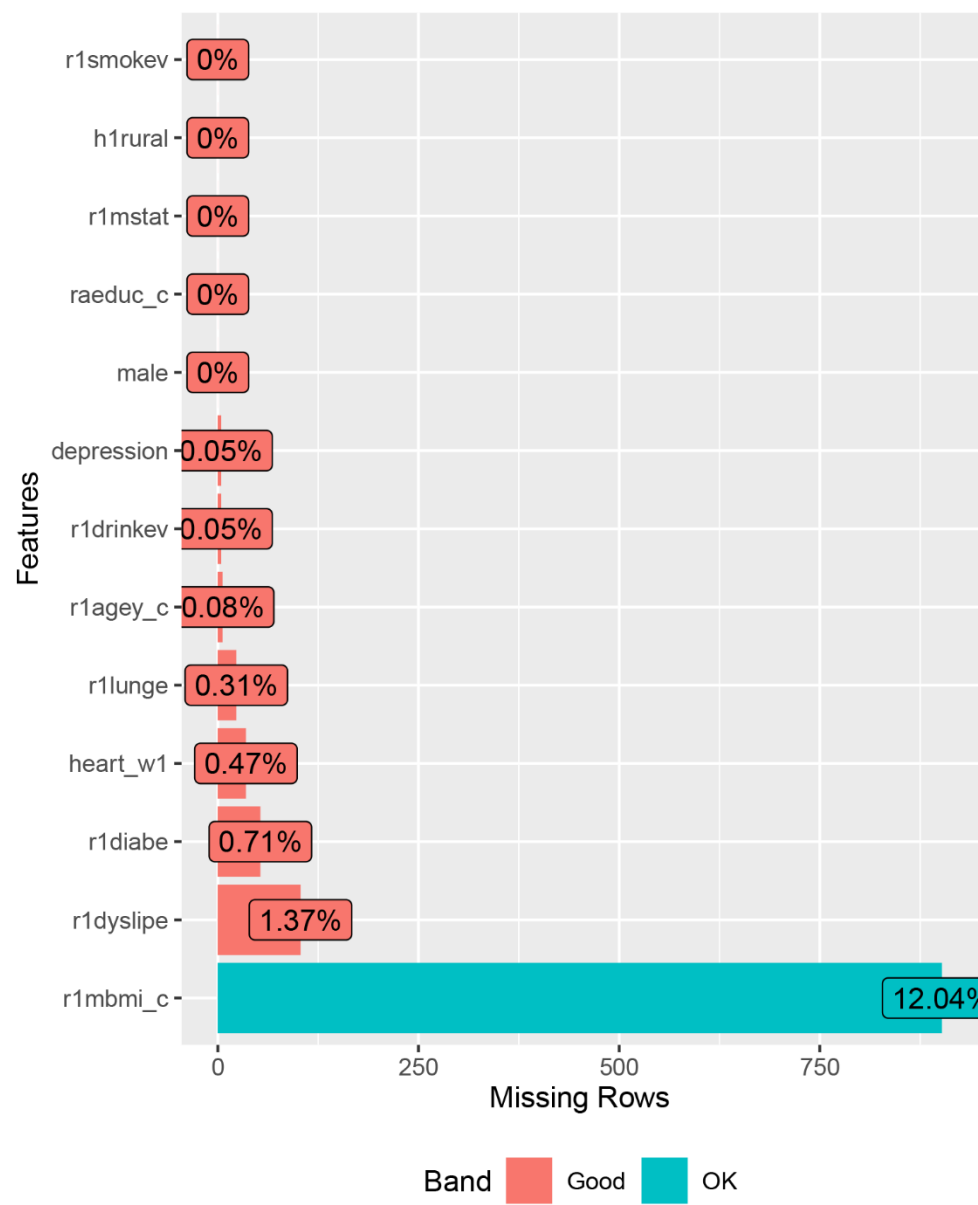


Figure S2. CHARLS Cohort Study Timeline

CHARLS Cohort Study Timeline

