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The Longitudinal Association Between Chronic Back Pain and Cognitive Decline in Older Adults With Mediation Analysis: An Analysis of Four Population-Based Databases

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ABSTRACT

Background: While studies suggest chronic back pain (CBP) may heighten accelerated cognitive decline risk in older adults, no multinational research has comprehensively examined this significant public health concern alongside healthy lifestyles' potential impact.

Methods: Data from 18,558 individuals across 17 countries (China, England, Europe, USA) were extracted from four databases (2010–2023; median follow-up: 8.4 years). Associations between CBP and memory-related diseases (MDs), cognitive function performance metrics (e.g., numeracy, orientation, immediate word recall, delayed word recall memory, and an overall cognitive score combining these elements), and subjective cognitive decline (SCD) were analysed using linear mixed-effects models and conducting mediation analysis through Structural Equation Modelling, adjusting for confounders.

Results: CBP significantly elevated MD and SCD risks in the USA (MDs: OR 1.03 to 1.47; SCD: OR 1.03 to 1.04) and Europe (MDs: HR 1.18 to 2.15; SCD: HR 1.01 to 1.03). Pooled meta-analyses confirmed significant but weak associations: MDs (OR = 1.35, 95% CI 1.03 to 1.68), delayed recall ($\beta = -0.05$, 95% CI −0.09 to −0.02), and SCD (HR = 1.02, 95% CI 1.00 to 1.03). Mediation analyses identified alcohol intake as exacerbating cognitive decline, while smoking cessation, physical activity, and sleep (7–9 h) reduced risks in older adults with CBP.

Conclusions: CBP heightens accelerated cognitive decline risks in older adults, mediated by modifiable lifestyle factors. These findings emphasise cognitive monitoring and tailored lifestyle interventions, particularly smoking cessation, activity promotion, and sleep optimisation in older adults with CBP. Multidimensional approaches integrating physical and behavioural strategies are critical to mitigating cognitive impairment in this population.

Significance Statement: CBP increases the risk of cognitive decline in older adults, underscoring the importance of preventing cognitive decline in this population. Public health initiatives should prioritise interventions that target CBP management and lifestyle modifications to mitigate the risk of pain and cognitive decline.

1 | Introduction

Chronic back pain (CBP), affecting either the upper or lower back, is a prevalent musculoskeletal disorder. Chronic low back pain, in particular, is the second largest contributor to rising healthcare costs (Dieleman et al. 2017). By 2050, it is projected that approximately 800 million people worldwide will experience chronic low back pain, placing a substantial economic burden on society (Ferreira et al. 2023). The prevalence of CBP increases with age, being most common among older adults (Patel et al. 2013), and can lead to poor self-rated health, fatigue, loneliness, and economic difficulties (Jacobs et al. 2006). With the global population aged 60 or older expected to increase from 1.4 billion to 2.1 billion by 2050 (Grinin et al. 2023), it is essential to address the negative impacts of CBP on older adults.

Research shows that older adults with CBP are more likely to experience subjective cognitive decline (SCD) and accelerated cognitive decline across various domains, such as attention, switching, and working memory than their asymptomatic counterparts (van der Leeuw et al. 2016). Such decline is concerning as it may precede dementia, profoundly impacting daily functioning (Livingston et al. 2020). Chronic pain is recognised as a risk factor for future cognitive decline among older adults (Whitlock et al. 2017). However, many cross-sectional (Grande-Alonso et al. 2023) and longitudinal studies (Whitlock et al. 2017) have focused on limited cognitive domains or have been conducted primarily in high-income countries, limiting their generalisability to broader demographics. As the prevalence of CBP varies significantly between low- or middle-income countries and high-income countries (GBD 2021 Forecasting Collaborators 2024), the relationship between CBP and cognitive decline may differ across individuals in countries with varying income or educational levels. However, it remains unclear which populations are particularly at risk for this association.

Considering that the association between CBP and cognitive decline may be influenced by various modifiable lifestyle factors, it is essential to understand their influences on the risk of cognitive decline among older adults with CBP. Previous research has indicated that individuals with chronic pain are more likely to consume alcohol (Ekholm et al. 2009) or smoke (Ditre et al. 2011), become physically inactive (van den Berg-Emons et al. 2007), and experience sleep disturbances (Chun et al. 2018). Light to moderate alcohol consumption has been associated with a lower risk of cognitive impairment (Zarezadeh et al. 2024), while excessive intake has the opposite effect (Yen et al. 2022). The likelihood of cognitive impairment may also vary among non-smokers, light smokers, and heavy smokers (Almeida et al. 2020). Additionally, individuals who get approximately 7 h of sleep per night tend to have optimal cognitive performance, whereas deviations from this sleep duration may lead to decreased cognitive function (Tai et al. 2022). Furthermore, regular physical exercise enhances the neuroplasticity of specific brain structures, thereby supporting cognitive health (Hötting and Röder 2013). Understanding how these lifestyle behaviours mediate the relation between CBP and cognitive decline across different populations may help develop effective preventive and treatment strategies.

Against this background, the current study aimed to: (1) investigate the longitudinal association between CBP and cognitive decline in older adults, using data from four population-based databases covering 17 countries across Asia, European countries, and the United States; and (2) explore potential mediating effects of alcohol consumption, smoking, physical activity levels, and sleep duration on this relationship.

2 | Materials and Methods

2.1 | Study Design and Participants

This study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines (von Elm et al. 2007). It was a longitudinal multi-cohort study using data from four databases involving various nationally representative ageing cohorts: the China Health and Retirement Longitudinal Study (CHARLS) (Zhao et al. 2014) from an upper-middle-income country, as well as the English Longitudinal Study of Ageing (ELSA) (Steptoe et al. 2013), the Health and Retirement Study (HRS) (Sonnega et al. 2014), and the Survey of Health, Ageing and Retirement in Europe (SHARE) (Börsch-Supan et al. 2013) from high-income countries. Each cohort involved biennial longitudinal studies with nationally representative samples of middle-aged and older adults, providing information on back pain and cognitive function for individuals aged 60 and older. Each database setting is provided in Method S1. For this research, we extracted data on CBP and cognitive assessments from waves 1–5 of CHARLS (2011–2020), waves 7–10 of ELSA (2014/15–2021/23), waves 10–15 of HRS (2010–2020) and waves 5–8 of SHARE (2013/14–2019/20) given that these waves of each database provided relevant data on CBP and cognitive assessments. Individuals aged 60 or older, both with and without CBP, were included in the analyses. Respondents younger than 60 and those with SCD or memory-related diseases (MDs) (e.g., Alzheimer's disease or memory impairment) at baseline were excluded.

2.2 | Exposure

While none of the databases specifically investigated the presence of CBP, they all included two pain-related questions: "Are you often troubled with pain?" and "On what part of your body do you feel pain?" Data is collected biennially across all four databases. If a participant answered "yes" to the first question and "back" to the second in the initial wave, and provided the same responses in the subsequent wave, they were classified as having CBP (Treede et al. 2015), indicating persistent back pain for at

least 2 years. Older adults without any acute and chronic pain were classified as the control group (Method S2).

2.3 | Outcomes

To compare cognitive function assessment results across different databases, we identified seven common cognitive domains from each of the four databases (Method S3). The primary outcomes were MDs and cognitive function performance metrics (e.g., numeracy, orientation, immediate word recall, delayed word recall memory, and an overall cognitive score combining these elements). MDs encompass conditions such as Alzheimer's disease, cerebral atrophy, dementia, organic brain syndrome, Parkinson's disease, senility, or any other serious memory impairments. The secondary outcome was SCD (Jessen et al. 2020). Diagnoses followed the International Classification of Diseases (ICD) 10th edition: SCD (ICD-10 code: R41.81), MDs (ICD-10 code: none). SCD refers to a persistent decrease in cognitive ability as perceived by the individual, compared to their previously normal cognitive functioning, and is not associated with any acute event (Jessen et al. 2020). Poor cognitive performance was indicated by the presence of MDs, low performance scores, and the presence of SCD across all databases (Arlt 2013; Jessen et al. 2020; Jin et al. 2023). To compare cognitive domains across the four databases and ensure that the scores followed a normal distribution, cognitive function performance scores in each database were standardised by creating a z-score for each domain, calculated by subtracting the mean and dividing by the standard deviation of the corresponding categories (Andrade 2021). This approach has been adopted to calculate Z-scores for cognitive function performance (Ma et al. 2020). Follow-up commenced at baseline (i.e., the initial assessment visit when CBP was measured) and continued until the reporting of one of the primary outcomes or the withdrawal from the study, whichever occurred first.

2.4 | Mediators

Potential mediators considered in this study included alcohol consumption, smoking status, physical activity levels, and sleep duration. These variables were assessed at the baseline. Alcohol consumption and smoking status were dichotomised as "yes" or "no". Physical activity levels were categorised into light, moderate, and vigorous intensity levels according to the World Health Organisation 2020 guidelines (Bull et al. 2020). Sleep duration was measured as the average number of hours slept per day over a week. Participants' reported sleep durations were categorised for analysis as short (<7 h), normal (7–9 h), and long (>9 h) (Consensus Conference Panel 2015).

2.5 | Confounders

We employed merging strategies to address certain differing confounders, incorporating harmonised strategies for key covariates in the present study (Method S4). A directed acyclic graph (DAG) was used to identify confounders, forming the minimally sufficient adjustment set (MSAS), derived from literature and DAGitty software (Method S5 and Figure S1) (Digitale et al. 2022; Textor et al. 2011). Consequently, age, gender, body mass index, educational levels, alcohol consumption, smoking, and physical activity levels were selected as the MSAS.

2.6 | Statistical Analysis

Baseline characteristics were presented as medians with interquartile ranges for continuous variables, and as frequencies and percentages (%) for categorical variables. Missing data on exposure and outcome variables were excluded from the analysis. Little's test was applied to evaluate whether confounder data were missing completely at random (MCAR), with a p-value ≥ 0.05 suggesting MCAR (Little 1988). Missing data, whether MCAR or not, were addressed using Multiple Imputations Chained Equations of five estimated data sets with chained equations (Heymans and Twisk 2022; Kontopantelis et al. 2017).

Given the rare occurrence of MDs during follow-up in each database, we used multivariable generalised estimating equation binary logistic regression models to account for time-dependent effects (King and Zeng 2001). Results were presented as odds ratios (ORs) with 95% CI.

To evaluate the impact of CBP on cognitive function performance over time, we employed linear mixed-effects models (Peng and Lu 2012). The Benjamini-Hochberg procedure was applied to linear mixed-effects models to control the false discovery rate at 5% for multiple testing corrections (Benjamini and Hochberg 1995). These models encompassed confounders, repeated measures of the exposures and outcomes, and random slopes and intercepts for each individual. The model with the lowest Akaike's information criterion value was considered the best fit and was used (Peng and Lu 2012).

Moreover, to investigate the influence of CBP on the binary cognitive outcome of SCD over time, we used a time-varying Cox proportional hazards regression model, using multiple follow-up time points as the temporal scale (Hendry 2014). The proportional hazards assumption was checked through collinearity (variance inflation factor smaller than 10) and Schoenfeld residuals (all global Schoenfeld tests $p>0.05$ and slopes far from zero). Additionally, the proportional hazard assumption was graphically assessed using Schoenfeld residual plots (Schoenfeld 1982). This analysis provided statistical significance, regression coefficients (β), and hazard ratios (HRs) with 95% confidence intervals (CI). Model fit was evaluated using the likelihood ratio test. Three statistical models were used: Model One was a crude model. Model Two was adjusted for the MSAS based on a DAG model, and Model Three was fully adjusted for all confounders. Our results were drawn from Model Two (MSAS-adjusted model).

Random-effects meta-analyses were used to pool statistical results of outcomes and the corresponding 95% CI from different cohorts to derive overall effect estimates (Guolo and Varin 2017). The heterogeneity of effect estimates across cohorts was tested using the Cochran Q test and I^2 statistic (Ruppar 2020).

Mediation analysis was conducted using Structural Equation Modelling to mitigate the impact of interaction effects on the

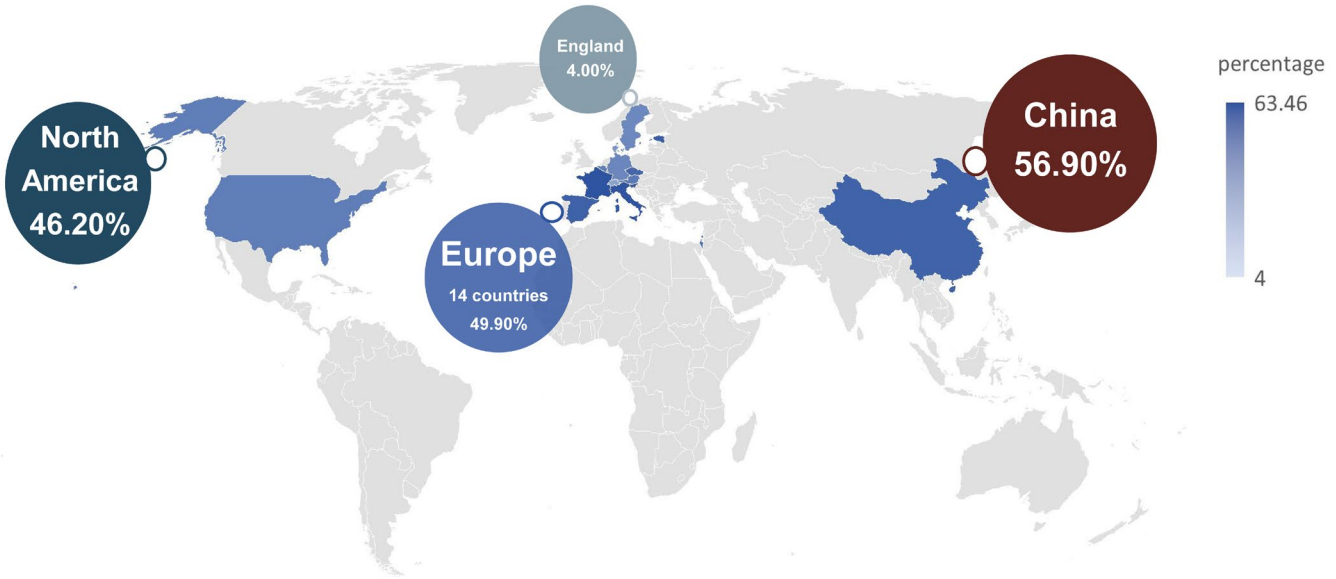

FIGURE 1 | Map of chronic back pain prevalence among older adults by country.

indirect effects (Valeri and Vanderweele 2013). The direct and indirect effects of Structural Equation Modelling, along with path coefficients, were reported (Valeri and Vanderweele 2013). We evaluated the model's fit using four widely recognised fit indices [the goodness of fit index, the adjusted goodness of fit index, the comparative fit index, and the root mean square error of approximation (RMSEA)] (Valeri and Vanderweele 2013).

As for sensitivity analysis, we first repeated the analysis using complete case analysis, excluding participants with missing data. We compare the results of the complete case analysis with those of the full sample analysis to assess the impact of missing data on the study results and to verify the robustness of the findings (Bartlett et al. 2014). Second, propensity score matching was performed using the nearest neighbour search strategy with a calliper of 0.02 to balance covariates between CBP groups and healthy controls. Matching was based on the MSAS score, ensuring balanced baseline characteristics at a 1:1 ratio. The balance of variables between CBP groups and healthy controls in each cohort before and after matching was assessed using the standardised mean difference, with values less than 0.10 indicating balance (Kane et al. 2020).

All statistical analyses were performed using SPSS 27.0 (IBM Corporation, Armonk, NY, USA), Stata 16 (Stata Corp LLC), and R version 4.2.2, with a two-tailed $p < 0.05$ indicating statistical significance.

3 | Results

3.1 | Baseline Characteristics of the Study Population

Participants were excluded if they were younger than 60 years old, did not have available data on age ($n = 57{,}638$), exposure ($n = 2909$), and outcomes ($n = 14{,}048$) in any of the four study cohorts. Meanwhile, data on pain other than CBP were excluded ($n = 11{,}371$), along with participants diagnosed with a memory-related disease, those who reported cognitive decline, or who experienced pain other than back pain ($n = 2979$). Ultimately, 18,558 participants (1812 from CHARLS, 1311 from ELSA, 7923 from HRS, and 7512 from SHARE) were included in the final analysis (Figure S2). The follow-up period ranged from eight to 10 years, with a median follow-up of 8.4 years. The prevalence of CBP in older adults varied widely across countries, ranging from 3.97% in England (ELSA) to 64.90% in Italy (SHARE) (Figure S3). CBP was reported by 1031 individuals (56.90%) from CHARLS, 52 participants (4.00%) from ELSA, 3658 individuals (46.20%) from HRS, and 3749 participants (49.90%) from SHARE at baseline. MDs were reported by no one (0%) from CHARLS, 45 participants (3.40%) from ELSA, 640 individuals (8.10%) from HRS, and 235 participants (3.10%) from SHARE during the same follow-up period. SCD was reported by 1456 individuals (80.40%) from CHARLS, 332 participants (25.30%) from ELSA, 2082 individuals (26.30%) from HRS, and 2313 participants (30.70%) from SHARE during the follow-up period (Figure 1; Table 1 and Tables S1–S3).

3.2 | The Causal Association Between CBP and MDs

Significant positive associations were observed between CBP in older adults and the incidence of MDs in HRS (OR = 1.23, 95% CI: 1.03 to 1.47) and SHARE (OR = 1.59, 95% CI: 1.18 to 2.15) (Table 2), while ELSA did not find any significant association. No cases of MDs were identified at either the baseline or during the follow-up period in CHARLS.

3.3 | The Causal Association Between CBP and Cognitive Function Performance Over a Median Follow-Up Period of 8.4 Years

The causal associations between CBP and various cognitive function performances with and without adjusting for

TABLE 1 | Characteristics of included participants in the CHARLS, ELSA, HRS, and SHARE.

	CHARLS ($n=1812$)	ELSA ($n=1311$)	HRS ($n=7923$)	SHARE ($n=7512$)
Age				
60–74	1591 (87.8%)	1078 (82.2%)	5109 (64.5%)	5079 (67.6%)
75–84	200 (11.0%)	221 (16.9%)	2260 (28.5%)	1997 (26.6%)
≥85	21 (1.2%)	12 (0.9%)	554 (7.0%)	436 (5.8%)
Gender				
Male	1222 (67.4%)	710 (54.2%)	3423 (43.2%)	3211 (42.7%)
Female	590 (32.6%)	601 (45.8%)	4500 (56.8%)	4301 (57.3%)
Body mass index, kg/m^2				
<18.5	136 (7.5%)	10 (0.8%)	31 (0.4%)	74 (1.1%)
18.5–24.9	1145 (63.2%)	370 (28.2%)	908 (11.5%)	2505 (33.3%)
25.0–29.9	446 (24.6%)	668 (50.9%)	2026 (25.6%)	3194 (42.5%)
≥30.0	85 (4.7%)	263 (20.1%)	4958 (62.5%)	1739 (23.1%)
Education				
Less than upper secondary	1659 (91.6%)	11 (0.8%)	810 (10.2%)	2794 (37.1%)
Upper secondary and vocational training	118 (6.5%)	933 (71.2%)	3436 (43.4%)	3053 (40.6%)
Tertiary	35 (1.9%)	367 (28.0%)	3677 (46.4%)	1665 (22.3%)
Marital status				
Married or partnered	1484 (81.9%)	815 (62.2%)	4970 (62.7%)	4280 (57.0%)
Others	328 (18.1%)	496 (37.8%)	2953 (37.3%)	3232 (43.0%)
Household wealth				
Low tertile	558 (30.8%)	322 (24.6%)	2608 (32.9%)	2431 (32.3%)
Medium tertile	636 (35.1%)	480 (36.6%)	2697 (34.0%)	2515 (33.4%)
High tertile	618 (34.1%)	509 (38.8%)	2618 (33.0%)	2566 (34.3%)
Working status				
Employed	69 (3.8%)	130 (10.0%)	1897 (23.9%)	920 (12.2%)
Unemployed	1743 (96.2%)	1181 (90.1%)	6026 (76.1%)	6592 (87.8%)
Lifestyle behaviours				
Alcohol consumption	559 (30.8%)	1222 (93.2%)	4230 (53.4%)	5431 (72.2%)
Smoking	775 (42.8%)	105 (8.0%)	962 (12.1%)	1304 (17.3%)
Social activities	910 (50.2%)	1258 (96.0%)	6226 (78.6%)	6933 (92.2%)
Physical exercise	665 (36.7%)	1291 (98.5%)	7408 (93.5%)	4131 (54.9%)
Sleep duration (hours)	6.27 (1.84)	7.00 (1.12)	6.32 (2.95)	7.02 (1.32)
Medical history				
Ever had physical disabilities	0 (0%)	460 (35.1%)	721 (9.1%)	4042 (53.8%)
Ever had hypertension	507 (28.0%)	64 (4.9%)	5174 (65.3%)	3533 (47.0%)
Ever had diabetes	99 (5.5%)	23 (1.8%)	1952 (24.6%)	1095 (14.5%)
Ever had cancer	172 (9.5%)	32 (2.4%)	1509 (19.0%)	701 (4.3%)

(Continues)

TABLE 1 | (Continued)

	CHARLS ($n=1812$)	ELSA ($n=1311$)	HRS ($n=7923$)	SHARE ($n=7512$)
Ever had chronic lung disease	172 (9.5%)	9 (0.7%)	915 (11.5%)	541 (7.2%)
Ever had heart problem	242 (13.4%)	66 (5.0%)	2340 (29.5%)	1028 (13.6%)
Ever had stroke	44 (2.4%)	10 (0.8%)	518 (6.5%)	297 (3.9%)
Ever had emotional, nervous or psychiatric problems	22 (1.2%)	5 (0.4%)	1287 (16.2%)	399 (5.3%)
Ever had sleep problems	849 (46.9%)	178 (13.6%)	7408 (93.5%)	2651 (35.2%)
Ever had arthritis or rheumatism	504 (27.8%)	37 (2.8%)	5357 (67.6%)	1643 (21.8%)
Chronic back pain	1031 (56.9%)	52 (4.0%)	3658 (46.2%)	3749 (49.9%)
Cognitive decline				
Subjective cognitive decline	1456 (80.4%)	332 (25.3%)	2082 (26.3%)	2313 (30.7%)
Memory-related disease	0 (0%)	33 (2.5%)	633 (8.0%)	235 (3.1%)
Numeracy	2.78 (2.04)	3.79 (1.79)	3.13 (1.80)	3.97 (1.56)
Orientation	3.72 (1.41)	3.83 (0.47)	3.77 (0.52)	3.89 (0.45)
Immediate word recall	3.18 (1.78)	6.40 (1.58)	9.23 (0.99)	5.23 (1.61)
Delayed word recall memory	2.58 (1.96)	5.17 (1.90)	8.95 (1.20)	3.85 (2.02)
An overall cognitive score	11.96 (5.45)	19.19 (4.23)	25.08 (3.00)	11.96 (5.45)

Note: Data are *n* (%) for categorical variables or mean (standard deviation) for continuous variables.
Abbreviations: CHARLS, China Health and Retirement Longitudinal Study; ELSA, English Longitudinal Study of Ageing; HRS, Health and Retirement Study; SHARE, Survey of Health, Ageing and Retirement in Europe.

TABLE 2 | Associations between chronic back pain and memory-related diseases in older adults.

		ELSA		HRS		SHARE	
Cognitive domain	**Model**	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***
Memory-related diseases	Model 1[a]	3.00 (0.89, 10.10)	0.08	1.22 (1.02, 1.46)	**0.03***	1.72 (1.30, 2.28)	**<0.001****
	Model 2[b]	1.94 (0.66, 5.73)	0.23	1.23 (1.03, 1.47)	**0.02***	1.59 (1.18, 2.15)	**0.002***
	Model 3[c]	0.67 (0.09, 4.81)	0.69	1.14 (0.95, 1.36)	0.17	1.39 (1.02, 1.90)	**0.04***
	Model 4[d]	1.16 (0.21, 6.36)	0.87	1.03 (0.87, 1.23)	0.70	0.54 (0.26, 0.82)	**<0.001****

Note: The *p*-value in bold indicates a statistically significant difference between chronic back pain with cognitive decline ($p<0.05$).
Abbreviations: CHARLS, China Health and Retirement Longitudinal Study; CI, confidence interval; ELSA, English Longitudinal Study of Ageing; HRS, Health and Retirement Study; OR, odd ratio; SHARE, Survey of Health, Ageing and Retirement in Europe.
[a]Model 1 is a crude model.
[b]Model 2 is adjusted for the minimal sufficient adjustment set (MSAS) identified using a causal directed acyclic graph (DAG) including age, gender, body mass index, educational levels, alcohol consumption, smoking, and physical activities based on Model 1.
[c]Model 3 builds upon Model 2 by incorporating health history factors, including the presence of physical disabilities, hypertension, diabetes, cancer, chronic lung disease, heart problems, stroke, emotional or psychiatric issues, sleep problems and arthritis or rheumatism.
[d]Model 4 builds upon Model 3 by incorporating medication use, including medication for high cholesterol, high blood pressure, diabetes, heart problems, osteoporosis, chronic lung diseases, digestive disorders, anxiety, depression, sleep issues, and inflammation (glucocorticoids or steroids).
*$p<0.05$.
**$p<0.001$.

confounders were presented in Table 3. As not all databases assessed the same cognitive domains, we reported associations based solely on the available data. CBP was negatively related to numeracy performance in CHARLS ($\beta=-0.06$, 95% CI: −0.12 to −0.01), ELSA ($\beta=-0.58$, 95% CI: −0.79 to −0.38), HRS ($\beta=-0.07$, 95% CI: −0.10 to −0.04), and SHARE ($\beta=-0.07$, 95% CI: −0.10 to −0.04). Likewise, CBP was associated with lower orientation scores, with MSAS-adjusted model estimates of ($\beta=-0.10$, 95% CI: −0.16 to −0.03 in CHARLS and $\beta=-0.04$, 95% CI: −0.06 to −0.02) in SHARE. Older adults with CBP showed significantly more decline in immediate word recall in CHARLS ($\beta=-0.08$, 95% CI: −0.13 to −0.02). Furthermore, significant declines in both immediate and delayed word recall memory were observed in older adults with CBP in ELSA and SHARE. The MSAS-adjusted model estimates were $\beta=-0.361$ (95% CI: −0.56 to −0.17) and $\beta=-0.06$ (95% CI: −0.09 to −0.03) for immediate recall, as well as $\beta=-0.25$ (95% CI: −0.45 to −0.05) and $\beta=-0.08$

TABLE 3 | Association between chronic back pain and cognitive decline (i.e., numeracy, orientation, immediate word recall, delayed word recall memory, and overall cognitive score) in older adults.

		CHARLS		ELSA		HRS		SHARE	
Mixed linear models		**β (95% CI)**	***p***	**β (95% CI)**	***p***	**β (95% CI)**	***p***	**β (95% CI)**	***p***
Numeracy	Model 1[a]	-0.09 (−0.15, −0.03)	**0.004***	−0.65 (−0.85, 0.44)	**<0.001****	−0.11 (−0.15, −0.08)	**<0.001****	−0.12 (−0.15, −0.09)	**<0.001****
	Model 2[b]	−0.06 (−0.12, −0.01)	**0.03***	−0.58 (−0.79, −0.38)	**<0.001****	−0.07 (−0.10, −0.04)	**<0.001****	−0.07 (−0.10, −0.04)	**<0.001****
	Model 3[c]	v0.04 (−0.10, 0.01)	0.14	−0.47 (−0.67, −0.27)	**<0.001****	−0.06 (−0.09, −0.02)	**<0.001****	−0.05 (−0.08, −0.02)	**0.002***
	Model 4[d]	−0.07 (−0.17, 0.04)	0.36	−1.11 (−1.54, −0.69)	**<0.001****	−0.07 (−0.14, −0.01)	0.07	−0.05 (−0.08, −0.02)	**0.002***
Orientation	Model 1[a]	−0.12 (−0.19, −0.06)	**<0.001****	−0.14 (−0.32, 0.05)	0.16	−0.01 (−0.04, 0.02)	0.43	−0.06 (−0.08, −0.03)	**<0.001****
	Model 2[b]	−0.10 (−0.16, −0.03)	**0.002***	−0.08 (−0.27, 0.11)	0.41	−0.01 (−0.04, 0.02)	0.44	−0.04 (−0.06, −0.02)	**<0.001****
	Model 3[c]	−0.08 (−0.14, −0.02)	**0.01***	0.05 (−0.12, 0.21)	0.60	−0.00 (−0.03, 0.02)	0.77	−0.03 (−0.01, −0.01)	**0.007***
	Model 4[d]	−0.11 (−0.20, −0.02)	0.05	0.02 (−0.09, 0.13)	0.85	−0.00 (−0.02, 0.02)	0.93	−0.04 (−0.06, −0.01)	**0.008***
Immediate word recall memory	Model 1[a]	−0.09 (−0.15, −0.03)	**0.004***	−0.50 (−0.71, −0.28)	**<0.001****	0.01 (−0.02, 0.04)	0.44	−0.12 (−0.13, −0.09)	**<0.001****
	Model 2[b]	−0.08 (−0.13, −0.02)	**0.005***	−0.36 (−0.56, −0.17)	**<0.001****	0.02 (−0.01, 0.05)	0.21	−0.06 (−0.09, −0.03)	**<0.001****
	Model 3[c]	−0.06 (−0.12, −0.01)	**0.03***	−0.23 (−0.42, −0.04)	**0.02***	0.03 (−0.00, 0.06)	0.07	−0.02 (−0.05, 0.01)	0.13
	Model 4[d]	−0.12 (−0.22, −0.01)	0.15	−0.50 (−0.88, −0.12)	**0.04***	0.05 (0.01, 0.08)	0.02	−0.02 (−0.05, 0.01)	0.26
Delayed word recall memory	Model 1[a]	−0.05 (−0.10, 0.01)	1.75	−0.38 (−0.61, −0.16)	**<0.001****	−0.04 (−0.06, −0.00)	**0.02***	−0.14 (−0.17, −0.10)	**<0.001****
	Model 2[b]	−0.03 (−0.09, 0.02)	0.19	−0.25 (−0.45, −0.05)	**0.01***	−0.03 (−0.06, 0.00)	0.07	−0.08 (−0.11, −0.05)	**<0.001****
	Model 3[c]	−0.02 (−0.07, 0.03)	**0.03***	−0.15 (−0.35, 0.06)	0.16	−0.02 (−0.05, 0.01)	0.28	−0.04 (−0.07, −0.00)	**0.03***
	Model 4[d]	−0.06 (−0.20, 0.09)	0.76	−0.41 (−0.89, 0.07)	0.28	−0.01 (−0.06, 0.03)	0.71	−0.03 (−0.06, 0.00)	0.08
Overall cognitive score	Model 1[a]	−0.10 (−0.17, −0.04)	**0.002***	−0.62 (−0.85, −0.39)	**<0.001****	−0.08 (−0.11, −0.05)	**<0.001****	−0.17 (−0.20, −0.13)	**<0.001****
	Model 2[b]	−0.08 (−0.13, −0.02)	**0.009***	−0.48 (−0.69, −0.27)	**<0.001****	−0.05 (−0.08, −0.02)	**0.002***	−0.09 (−0.13, −0.06)	**<0.001****
	Model 3[c]	−0.06 (−0.12, 0.00)	0.05	−0.33 (−0.53, −0.13)	**0.001***	−0.03 (−0.06, −0.00)	0.05	−0.05 (−0.08, −0.02)	**0.003****
	Model 4[d]	−0.32 (−0.67, 0.03)	0.20	−1.99 (−3.09, −0.89)	**0.003***	−0.01 (−0.06, 0.03)	0.71	−0.05 (−0.08, −0.01)	**0.007****

Note: The *p*-value in bold indicates a statistically significant difference between chronic back pain and cognitive decline ($p < 0.05$).

Abbreviations: CHARLS, China Health and Retirement Longitudinal Study; CI, confidence interval; ELSA, English Longitudinal Study of Ageing; HRS, Health and Retirement Study; SHARE, Survey of Health, Ageing and Retirement in Europe; β, regression coefficient.

[a]Model 1 is a crude model.

[b]Model 2 is adjusted for the minimal sufficient adjustment set identified using a causal directed acyclic graph (DAG) including age, gender, body mass index, educational levels, alcohol consumption, smoking, and physical activities based on Model 1.

[c]Model 3 builds upon Model 2 by incorporating health history factors, including the presence of physical disabilities, hypertension, diabetes, cancer, chronic lung disease, heart problems, stroke, emotional or psychiatric issues, sleep problems and arthritis or rheumatism.

[d]Model 4 builds upon Model 3 by incorporating medication use, including medication for high cholesterol, high blood pressure, diabetes, heart problems, osteoporosis, chronic lung diseases, digestive disorders, anxiety, depression, sleep issues and inflammation (glucocorticoids or steroids).

*$p < 0.05$.

**$p < 0.001$.

(95% CI: −0.11 to −0.05) for delayed word recall, respectively. A significant negative association between CBP and overall cognitive scores was identified in CHARLS ($\beta = -0.08$, 95% CI: −0.13 to −0.02), ELSA ($\beta = -0.48$, 95% CI: −0.69 to −0.27), HRS ($\beta = -0.05$, 95% CI: −0.08 to −0.01) and SHARE ($\beta = -0.09$, 95% CI: −0.13 to −0.06). After controlling for the false discovery rate with the Benjamini-Hochberg procedure for multiple comparisons, our findings proved robust.

3.4 | The Causal Association Between CBP and SCD

CBP were significantly associated with a higher risk of incident SCD in both HRS (HR = 1.03, 95% CI: 1.03 to 1.04) and SHARE (HR = 1.02, 95% CI: 1.01 to 1.03) (Table 4), with no collinearity issues, all global Schoenfeld tests $p > 0.05$ and slopes far from zero (Figures S4–S10), while CHARLS and ELSA did not show any significant association.

3.5 | Meta-Analysis Results

The meta-analyses showed that baseline CBP increased the risk of MDs, with a pooled OR of 1.35 (95% CI: 1.03 to 1.68), and SCD, with a pooled HR of 1.02 (95% CI: 1.00 to 1.03) at follow-ups. Among various cognitive functions, a small negative association was found only between CBP and delayed word recall memory ($\beta = -0.05$, 95% CI: −0.09 to −0.02) (Figure S11).

3.6 | Mediation Results

3.6.1 | Alcohol Consumption

Alcohol consumption significantly mediated the indirect effect of CBP on overall cognitive scores across all databases except ELSA and SHARE (CHARLS: $\beta = 1.12$, 95% CI: 0.55 to 1.69; HRS: $\beta = 0.53$, 95% CI: 0.30 to 0.75). Additionally, in the SHARE, CBP indirectly affected SCD through alcohol consumption ($\beta = -0.06$, 95% CI: −0.09 to −0.04), suggesting that the effect of CBP on SCD was suppressed by more alcohol intake. The positive beta values indicated that the effects of CBP on overall cognitive scores were enhanced by alcohol consumption.

3.6.2 | Smoking

A significant indirect effect of CBP on overall cognitive scores through smoking ($\beta = 1.13$, 95% CI: 0.60 to 1.67) was found in CHARLS. This suggests that CBP significantly affected overall cognitive scores partially through its influence on smoking. However, the model fit was poor.

3.6.3 | Physical Activity Levels

In both the ELSA and SHARE, CBP significantly influenced overall cognitive scores indirectly through physical activity levels (ELSA: $\beta = 0.77$, 95% CI: 0.28 to 1.27; SHARE: $\beta = 0.37$, 95%

TABLE 4 | Associations between chronic back pain and subjective cognitive decline in older adults.

Cognitive domain	Model	CHARLS		ELSA		HRS		SHARE	
		HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*
Subjective cognitive decline	Model 1[a]	1.01 (1.00, 1.01)	0.05	0.98 (0.92, 1.05)	0.62	1.03 (1.03, 1.04)	**< 0.001****	0.78 (0.72, 0.85)	**< 0.001****
	Model 2[b]	1.01 (1.00, 1.01)	0.06	0.97 (0.91, 1.04)	0.41	1.03 (1.03, 1.04)	**< 0.001****	1.02 (1.01, 1.03)	**< 0.001****
	Model 3[c]	1.00 (0.99, 1.01)	0.23	0.97 (0.91, 1.04)	0.46	1.03 (1.02, 1.03)	**< 0.001****	1.01 (1.00, 1.02)	0.15
	Model 4[d]	0.08 (1.04, 1.14)	**< 0.001****	−0.14 (0.48, 1.58)	0.65	0.25 (1.22, 1.36)	**< 0.001****	0.21 (1.17, 1.31)	**< 0.001****

Note: The *p* in bold indicates a statistically significant difference between chronic back pain with cognitive decline ($p < 0.05$).
Abbreviations: CHARLS, China Health and Retirement Longitudinal Study; CI, confidence interval; ELSA, English Longitudinal Study of Ageing; HR, hazard ratio; HRS, Health and Retirement Study; SHARE, Survey of Health, Ageing and Retirement in Europe.
[a]Model 1 is a crude model.
[b]Model 2 is adjusted for the minimal sufficient adjustment set (MSAS) identified using a causal directed acyclic graph (DAG) including age, gender, body mass index, educational levels, alcohol consumption, smoking, and physical activities based on Model 1.
[c]Model 3 builds upon Model 2 by incorporating health history factors, including the presence of physical disabilities, hypertension, diabetes, cancer, chronic lung disease, heart problems, stroke, emotional or psychiatric issues, sleep problems and arthritis or rheumatism.
[d]Model 4 builds upon Model 3 by incorporating medication use, including medication for high cholesterol, high blood pressure, diabetes, heart problems, osteoporosis, chronic lung diseases, digestive disorders, anxiety, depression, sleep issues and inflammation (glucocorticoids or steroids).
**$p < 0.001$.

CI: 0.20 to 0.54). The model demonstrated a poor fit in ELSA, but an acceptable fit in SHARE.

3.6.4 | Sleep Duration

CBP indirectly affected MDs through sleep duration ($\beta = 0.003$, 95% CI: 0.001 to 0.004, $p < 0.001$) in SHARE. For short sleepers (< 7 h), shorter sleep duration amplified the detrimental effect of CBP on MDs ($\beta = -0.06$, 95% CI: −0.006 to −0.002, $p = 0.001$), with a robust model fit. Among normal sleepers (7–9 h), longer sleep duration provided an indirect protective effect ($\beta = 0.05$, 95% CI: 0.003 to 0.01, $p = 0.002$) against cognitive decline. Conversely, for long sleepers (> 9 h), there was no significant direct association between CBP and MDs.

The Structural Equation Model results showed that CBP indirectly affected MDs, overall cognitive scores, and SCD through alcohol consumption, smoking, physical activity levels, and sleep duration in some databases. However, in the HRS data, these factors were not significant mediators between CBP and MDs or SCD. Due to the lack of a significant direct association between CBP and MDs or SCD in CHARLS and ELSA, mediation analysis was not performed on these datasets. The model fit statistics across the four databases reveal varying degrees of fit, with CHARLS showing poor fit (RMSEA = 0.14), while ELSA and HRS exhibit acceptable to good fit (ELSA: RMSEA = 0.06; HRS: RMSEA = 0.06), and SHARE demonstrating consistent good fit (RMSEA = 0.04–0.05). Detailed mediation and mediation model fit results were shown in Tables S4–S8, and Figures S12–S15.

3.7 | Variations in CBP and Cognitive Decline in High- and Upper-Middle-Income Countries

In CHARLS, representing an upper-middle-income country, almost all older adults with CBP reported SCD during the follow-up periods (99.99%, 1030 out of 1031), while none reported MDs. Conversely, high-income regions represented by SHARE in Europe, such as Austria (47.96%, 400 out of 834), Belgium (46.44%, 411 out of 885), and Estonia (58.78%, 472 out of 803), showed lower frequencies of older adults with CBP reporting SCD. In ELSA data from England, three participants reported MDs, and 23 out of 52 participants with CBP reported SCD. The HRS data from the United States showed a high number of participants, with 320 out of 3658 reporting MDs, with CBP (2521 out of 3658) reporting SCD. Detailed results of regional differences were presented in Tables S2 and S3.

3.8 | Sensitivity Analysis

The sensitivity analysis using complete case analysis showed that the time-varying Cox proportional hazards regression models across four databases were consistent with the main analyses. In SHARE, the association between CBP and numeracy scores also remained significant. Furthermore, sensitivity results from propensity score matching for CBP and measures of numeracy, orientation, word recall memory, and overall cognitive scores among individuals from CHARLS, ELSA, and HRS aligned with the main analyses. Additional sensitivity analyses using propensity score matching revealed a positive association between CBP and MDs in HRS and SHARE. However, due to the limited sample size of MDs and CBP cases in ELSA, no cases were available for complete case analysis and propensity score matching (Tables S9–S12).

4 | Discussion

This study is the first intercontinental comparison study to investigate the causal association between CBP and future cognitive decline in older adults, using 17 national longitudinal datasets with a median follow-up period of 8.4 years. Our findings indicated that CBP was related to the onset of MDs and SCD in both Europe and the United States. Baseline CBP increased the risk of multidomain poor cognitive performance, including deficits in numeracy, orientation, word recall memory, and overall cognitive scores among individuals from China, England, the United States, and Europe during follow-ups. Exceptions were observed in orientation in England and the United States, as well as in immediate word recall memory in the United States and delayed word recall memory in both China and the United States. In the United States, baseline CBP was associated with future declines in orientation, immediate word recall, and delayed word recall memory. However, the magnitude of association is in general small and therefore our findings should be interpreted with caution.

Our included databases consistently classified Alzheimer's disease, cerebral atrophy, dementia, organic brain syndrome, Parkinson's disease, senility, and other severe memory impairments (both AD and non-AD-related) (Arlt 2013) as MDs. In ELSA, three individuals with CBP were diagnosed with MDs at follow-up, aligning with incidence rates reported in previous research (Yiengprugsawan and Steptoe 2018). However, CHARLS did not identify any MD cases at baseline or follow-up. The absence of MD cases in China may be due to the underdiagnosis of MD among older adults with cognitive impairment, especially in socioeconomically deprived subgroups (Qian et al. 2021). As MD increase mortality rates and reduce life expectancy (Liang et al. 2021), our findings highlight the importance of monitoring and early diagnosing MD in older adults with CBP.

Our findings revealed that older adults with CBP showed significant cognitive decline in performance metrics across various ancestries and continents. Age-related declines in numeracy, exacerbated by CBP, can impair an individual's capacity to make informed decisions, including health and financial management, which rely on understanding numerical data (Best et al. 2022). Low numeracy can also skew risk perception, reduce medication compliance, and hinder effective risk communication, all critical for informed medical decision-making (Chen et al. 2014). Additionally, chronic pain is associated with cognitive decline in orientation due to hippocampal atrophy (Zhao et al. 2024). Older adults with impaired spatial orientation may become disoriented in familiar settings, increasing safety risks, anxiety, and embarrassment, which can lead to social withdrawal and loneliness (Plácido et al. 2022). Further, persistent pain is related to a faster decline in word

recall memory among older adults (Whitlock et al. 2017), as it depletes cognitive resources and hinders individuals' ability to devote adequate attention and memory capacity to recall words or information (Chen et al. 2023). It also damages brain structures associated with memory, especially the hippocampus (Xia et al. 2020).

Prior research indicates that individuals with chronic pain have a higher incidence of SCD (15.2%) compared to age-matched healthy controls (Taylor et al. 2018), with 16.3% of those with moderate joint pain and 28.5% of those with severe pain reporting SCD (Horgas et al. 2022). Given that SCD increases the risk of future cognitive decline and dementia (Jessen et al. 2020), both previous and current findings consistently emphasise the importance of pain management in older adults with CBP.

In the SHARE cohort, alcohol consumption was associated with reduced SCD complaints among individuals with CBP, suggesting that non-drinkers with CBP may be more aware of their SCD than drinkers. However, since SCD was subjectively reported, this could introduce bias (Jessen et al. 2014). Alcohol consumption also indirectly enhanced the negative effects of CBP on overall cognitive scores in the CHARLS, HRS, and SHARE cohorts. These findings suggest that older adults with CBP who consume alcohol may experience less cognitive decline. A systematic review indicates a significant J-shaped association between alcohol consumption and cognitive dysfunction, where light to moderate intake may offer protective benefits, while excessive consumption increases the risk of cognitive decline (Zarezadeh et al. 2024). However, our included databases only inquired whether participants consumed alcohol, making it impossible to examine the dose effect.

Smoking was found to mediate the association between CBP and lower overall cognitive scores only in the CHARLS cohort not in the other three databases. This discrepancy may be attributed to the higher prevalence of smoking in CHARLS. In China, the smoking rate among older adults is 25.6% (Yuan et al. 2022), which is higher than that in countries in the other three datasets (West 2017). Research has revealed that individuals with chronic pain are more likely to smoke as a coping mechanism (Ditre et al. 2011), and smoking is related to accelerated cognitive decline (Benito-León et al. 2023). The higher smoking rate in CHARLS may increase the statistical power to identify smoking as a significant mediator between CBP and cognitive dysfunction, particularly in populations with high smoking prevalence. Therefore, public campaigns targeting smokers could be important for improving cognitive function in this high-risk group.

Increased physical activity improves cognitive function. Mediation analysis of the ELSA and SHARE datasets showed that higher physical activity levels are related to better cognitive performance in individuals with CBP. Engaging in appropriate physical activity promotes neurogenesis, synaptogenesis, angiogenesis, and the release of neurotrophins, thereby promoting cognitive function (Hötting and Röder 2013). However, older adults with CBP often experience balance control issues, making it difficult to participate in physical exercise (Zheng et al. 2024). Clinicians should tailor exercise prescriptions to the balanced abilities of older adults with CBP.

Our findings from the SHARE cohort suggest that maintaining a normal sleep duration (7–9 h) was important for reducing the risk of MDs, consistent with previous research (Ma et al. 2020). Insufficient sleep directly promotes amyloid protein accumulation and synaptic damage (Wang et al. 2024), while prolonged sleep can indirectly impair cognitive function through increased systemic inflammation (Wu and Xu 2020). A normal sleep duration may mediate the relationship between CBP and MDs by protecting against pathological protein deposition (Winer et al. 2021) and degenerative changes in brain structures (Tang et al. 2024).

The impact of CBP on cognitive decline among older adults differed between high- and middle-income countries and cultures. While no cases of MDs were reported in CHARLS, some were noted among older adults with CBP in high-income regions during follow-up. Many developed countries have national strategies focusing on risk mitigation, early intervention, and public health campaigns to raise dementia awareness and improve access to treatment (Hampel et al. 2022). Conversely, cognitive decline and dementia receive limited public health attention in China (Jia et al. 2020), with less than 6% of affected older adults seeking medical consultation and treatment (Jiang et al. 2024). In CHARLS, older adults with CBP reported a higher rate of SCD at follow-up compared to those in other Western databases. This difference could be ascribed to greater public awareness and reduced stigmatisation of cognitive health issues in Western countries, where public health information is frequently updated based on new research findings (Tang and Peng 2015). Consequently, Western countries may report lower SCD rates due to a stronger emphasis on early detection and treatment.

5 | Strengths and Limitations

Our study has several strengths. First, it used large-scale population-based multi-cohort databases from 17 high- and middle-income countries, with nationally representative samples of older populations in each region. Second, we employed meta-analyses to synthesise the results, providing comprehensive and representative findings. Third, this study is the first to explore whether the association between CBP and cognitive decline in older adults is mediated by factors such as alcohol consumption, smoking, physical activity levels, and sleep duration.

When interpreting our results, several limitations should be considered. First, CBP is a subjective experience influenced by individual factors such as biopsychosocial interactions, which may introduce biases (Fillingim 2017). Second, while chronic pain is generally defined as pain persisting for at least 3 months (Scholz et al. 2019), our study defines CBP as back pain reported for at least 2 years due to database constraints. This definition may introduce ambiguity, considering the temporal variability of pain and the possibility of referred pain from visceral organs (Vera-Portocarrero and Westlund 2005). Third, in all the databases we included, MDs encompass a range of memory-related disorders. However, the lack of clear definitions for each condition adds to the ambiguity in diagnosing MDs. Fourth, one of our outcome measures, SCD, reflects patients' perceived decline in memory capabilities (Jessen et al. 2014). However, without an objective diagnosis, its clinical diagnostic value is limited (Pavel

et al. 2022). Fifth, the limited precision of disease classification in our databases, specifically the inability to exclude mild cognitive impairment, identify distinct cases of Parkinson's disease, or verify the reliability of electronic diagnoses, may lead to some degree of heterogeneity in the outcomes. Sixth, older adults with CBP have poorer overall health and may present with various comorbidities and psychosocial risk factors that could contribute to cognitive decline. In our analyses, we recognise that we only controlled for measurable and available confounders, which limits our ability to fully isolate the effects of CBP.

6 | Conclusions

CBP increases the risk of accelerated cognitive decline in older adults, with alcohol consumption, smoking, physical activity levels, and sleep duration acting as mediators. These findings underscore the importance of monitoring cognitive function and promoting a healthy lifestyle in older adults with CBP. However, it is essential to recognise the multifactorial nature of cognitive deficits in older adults. Future research is warranted to investigate the negative effects of other types of chronic pain in older adults and conduct similar longitudinal studies in low-income countries.

Author Contributions

F.F.H.: Conceptualisation, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, resources, software, supervision, validation and writing – original draft; Y.Z.: Conceptualisation, data curation, formal analysis, methodology, software and writing – original draft; L.L.: Conceptualisation, data curation, formal analysis, methodology and writing – original draft; C.L.H.: Conceptualisation, writing – review and editing; R.C.: Data curation, writing – review and editing; W.W.: Data curation, writing – review and editing; D.K.Y.Z.: Writing – review and editing; Z.X.: Writing – review and editing; J.R.C.: Writing – review and editing; Y.Z.: Writing – review and editing; M.L.F.: Writing – review and editing; P.H.F.: Writing – review and editing; F.U.A.: Writing – review and editing; F.A.L.Z.: Writing – review and editing; H.T.L.: Writing – review and editing; A.Y.L.W.: Writing – review and editing.

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Conflicts of Interest

The authors declare no conflicts of interest.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Data S1:** ejp70084-sup-0001-Supinfo.docx.