BMJ Open

Association between serum 25-hydroxyvitamin D levels and cognitive function among older adults in Tianjin, China: a cross-sectional community-based study

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To cite: Lou Z, Han X, Wu X, *et al*. Association between serum 25-hydroxyvitamin D levels and cognitive function among older adults in Tianjin, China: a cross-sectional community-based study. *BMJ Open* 2026;**16**:e115914. doi:10.1136/bmjopen-2025-115914

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2025-115914).

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Received 25 December 2025
Accepted 21 July 2026

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ABSTRACT

Objective To explore the association between serum 25-hydroxyvitamin D (25-OH-D) levels and mild cognitive impairment (MCI) and further analyse the association between serum 25-OH-D levels and different dimensions of cognitive function.

Design Cross-sectional study.

Setting Tianjin, China.

Participants A total of 866 participants aged 65 and above were enrolled in this study.

Outcome MCI was diagnosed based on the revised Petersen diagnostic criteria. Cognitive function was assessed by the Wechsler Adult Intelligence Scale Revised in China.

Results The prevalence of MCI was 12.0%. Higher serum 25-OH-D levels were significantly associated with lower odds of MCI, as well as with MCI across all subgroups ($p<0.05$). Serum 25-OH-D levels were significantly and positively associated with full intelligence quotient (FIQ), verbal intelligence quotient (VIQ), information, similarity and vocabulary ($p<0.05$). The associations between serum 25-OH-D levels and cognitive function did not significantly differ by age, gender or education level, with no statistical evidence of interactive effects.

Conclusion Higher serum 25-OH-D levels were significantly associated with lower odds of MCI. Furthermore, serum 25-OH-D levels were significantly and positively associated with different dimensions of cognitive function, specifically FIQ, VIQ, information, similarity and vocabulary. There was no statistically significant interaction observed between serum 25-OH-D levels and age, gender or education level.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The use of strict diagnostic criteria for mild cognitive impairment (MCI) enhanced the reliability of the survey outcomes.
⇒ The adoption of the Wechsler Adult Intelligence Scale Revised in China (WAIS-RC), a cognitive assessment tool culturally adapted and standardised for Chinese populations, ensured precise measurement of cognitive function.
⇒ The study systematically examined the association between serum 25-hydroxyvitamin D (25-OH-D) levels and different dimensions of cognitive function.
⇒ A cross-sectional study is limited in its ability to infer causal relationships between serum 25-OH-D levels and cognitive function
⇒ The samples in this study were only from the Tianjin area, which limits the extrapolation of the results to a certain extent.

INTRODUCTION

In recent years, the global prevalence of Alzheimer's disease (AD) has risen concurrently with population ageing, positioning it as the most prevalent form of senile dementia. Epidemiological evidence underscores that individual older adults face a substantially elevated risk of developing AD.[1] Statistics indicate that by 2023, there have already been approximately 9.83 million patients with AD in China.[2] This escalating prevalence not only strains national healthcare systems but also imposes profound socioeconomic and psychological burdens on families. Despite extensive research, no disease-modifying pharmacological therapies have been established for AD to date. Consequently, prioritising preventive interventions prior to clinical onset represents a pragmatic and cost-effective strategy to mitigate the societal and individual burdens of this debilitating condition.

Mild cognitive impairment (MCI) represents an intermediate stage between normal ageing and AD, characterised by an increased risk of progression to dementia. As a critical gateway for early AD prevention, implementing timely intervention during the MCI stage can effectively delay dementia progression.[3] The prevalence of MCI increases with advancing age,[4] with approximately 15% of MCI patients progressing to AD within 2 years.[5] These findings showed the substantial public health significance of early

MCI prevention in China. MCI is characterised by multifaceted cognitive impairments including deficits in perception, attention,[6] memory, thinking ability, language ability,[7] learning ability and executive function.[8] These cognitive domains can be evaluated through a series of neuropsychological tests. Specifically, the Wechsler Adult Intelligence Scale Revised in China (WAIS-RC) is a commonly used tool for assessing cognitive function in older adults, providing a multidimensional assessment.

Epidemiological studies suggest that targeted nutritional interventions may mitigate the progression of cognitive decline. It is hypothesised that nutrients, including vitamins, may influence the risk of developing future cognitive impairment and dementia.[9] Vitamin D has important physiological functions as an essential fat-soluble steroidal vitamin. Vitamin D is available in the form of ergocalciferol (vitamin D_2) and cholecalciferol (vitamin D_3).[10] Vitamin D undergoes two hydroxylation processes in the body; it first undergoes hydroxylation in the liver by 25-hydroxylase to generate serum 25-hydroxyvitamin D (25-OH-D). Subsequently, it is further hydroxylated in the kidney to form the active metabolite, 1,25-dihydroxyvitamin D. Serum 25-OH-D levels are now a recognised marker of vitamin D status.[11] The older adults exhibit heightened susceptibility to vitamin D insufficiency due to age-related declines in cutaneous synthesis, dietary intake, absorption efficiency and metabolic activation.[11 12] Globally, vitamin D deficiency affects an estimated one billion individuals, underscoring its status as a critical public health challenge.[12] The study conducted among community-dwelling older adults has shown that there were significant associations between low levels of serum 25-OH-D and MCI and cognitive decline.[13] Vitamin D can prevent cognitive impairment in several ways, including inhibiting chronic inflammatory responses, antioxidant effects and plaque clearance and promoting synthesis of neurotrophic factors.[14–16] These non-specific neuroprotective mechanisms are crucial not only for healthy cognitive ageing but also across various neurological conditions, such as multiple sclerosis and other neurodegenerative diseases. While some research supports serum 25-OH-D levels are associated with memory and cognitive functions,[17] others have demonstrated no significant association.[18]

Based on the inconsistency of the above findings and the comprehensive conclusions of previous studies on different populations, the present study was conducted to explore the association between serum 25-OH-D levels and MCI in a cross-sectional study among the older adults in Tianjin; on this basis, the association between serum 25-OH-D levels and different dimensions of cognitive function was explored in conjunction.

SUBJECTS AND METHODS

Research subjects

Selection of research subjects

In this study, a cluster sampling method was employed to select four communities: Yuanyinli Community, Yingshuili Community, Yingjiangxili Community and Baoshanbeili Community under Wangdingdi Street's jurisdiction in Tianjin, China. All older adults aged 65 and above in these four communities were enrolled as study subjects. The research was conducted from March to June 2016. The flow chart of this cross-sectional study is detailed in online supplemental figure 1.

Sample size estimation

Based on the prevalence of MCI in the literature (p=0.114),[19] taking $z_{1-\alpha/2}$= 1.96 and allowable error δ= 0.03, according to the formula: $n = \left(\frac{Z_{1-\alpha/2}}{\delta}\right)^2 \times P \times (1-P)$, the minimum sample size was 408, and taking into account 10% missing data, the final required sample was 449. 866 older people aged 65 and above were ultimately enrolled in the survey, confirming that the sample size met the research requirements.

Inclusion and exclusion criteria

Inclusion criteria: (1) aged ≥65 years and having resided in the selected community for more than 2 years; (2) willing to participate voluntarily and cooperate actively in completing the survey.

Exclusion criteria: (1) severe perceptual deficits that prevented assessment of cognitive function; (2) significant hearing or speech communication deficits; to prevent sensory impairments from confounding the performance subtests, participants who could not clearly see or hear the testing materials even with corrective aids (such as glasses or hearing aids) were strictly excluded. For eligible participants with mild-to-moderate age-related sensory decline, assessments were conducted using standard large-font visual materials and clear vocal amplification to ensure sensory limitations did not confound their test performance; (3) psychiatric disorders or recent (within 3 months) use of medications that affect cognitive function, or current use of vitamin D supplements and related medications affecting bone and vitamin D metabolism.

Diagnosis of mild cognitive impairment

Based on the Petersen diagnostic criteria[20] and considering China's actual situation, the diagnostic criteria for MCI were revised and defined as follows: (1) participants reported subjective memory decline or family members/physicians objectively confirmed memory impairment; (2) memory loss persisted for at least 3 months; (3) Mini-Mental State Examination scores: illiterate group ≤17 points; primary school education group ≤20 points; middle school and above education group ≤24 points; (4) slight impairment in activities of daily living, with an Activity of Daily Living assessment score ≤26;[21] exclusion of senile dementia, AD and other diseases causing cognitive dysfunction.

Questionnaire survey

The study employed the 'Health Status Questionnaire for the Community-based Older Adult in Tianjin'[22] to conduct face-to-face questionnaire surveys. All investigators were uniformly and standardly trained before collecting the questionnaires. The content of the questionnaire survey covered two major

parts: basic demographic characteristics and health status. The basic demographic characteristics include age, gender, education level (bachelor's degree and above, high school and below). Health conditions include current diseases and history of hypertension, type 2 diabetes, heart disease and stroke; disease history was self-reported based on physician diagnoses, adhering to international diagnostic standards.

Blood pressure measurement

Participants rested quietly for at least 5 min. Their sitting blood pressure was measured using an arm-type medical electronic sphygmomanometer (Omron HBP-9020). After a 1–2-minute interval, measurements were repeated, and the clinic blood pressure value was calculated as the average of three readings.

Assessment of cognitive function

The study used the WAIS-RC to assess the intelligence of the research subjects. The WAIS-RC consists of two parts: the verbal subtest and the performance subtest. The verbal subtest includes six dimensions: information, comprehension, arithmetic, similarity, digit span and vocabulary; the performance subtest includes five dimensions: digit symbol, picture completion, block design, picture arrangement and object assembly.[23] To minimise examiner dependence and guarantee data quality, all neuropsychological assessments were conducted face-to-face by two uniformly trained investigators from our research team. The inter-rater reliability between the two examiners was rigorously evaluated, demonstrating an excellent consensus. Furthermore, all interviews were conducted in quiet, well-lit community rooms to minimise environmental distractions. Participants were administered the tests in a standardised order, starting with verbal and then performance dimensions. Raw scores from each dimension were converted to standard scaled scores for comparative analysis. After obtaining scaled scores for all dimensions, the Verbal and Performance Index Scores were calculated by summing relevant dimension scores. Concurrently, the total test score was computed. Finally, using the age-corresponding IQ conversion table, verbal intelligence quotient (VIQ), performance intelligence quotient (PIQ) and full intelligence quotient (FIQ) were determined by integrating the two index scores and total score.

Laboratory testing

Collection of blood samples

Venous blood samples were collected from all participants between 8:00 AM and 10:00 AM after a required overnight fasting period of at least 8 hours. Two tubes of 4 mL venous blood were collected in the early morning under fasting conditions. Blood samples were processed using polypropylene coagulation tubes and ethylenediaminetetraacetic acid anticoagulant tubes. For coagulation tubes, supernatants were obtained at 4 °C (3000 rpm for 10 min), then stored at −80°C. Anticoagulant tubes were centrifuged at 2500 rpm for 10 min, followed by direct aliquoting and storage at −80°C. Total cholesterol (TC) was measured using an enzymatic method on a Beckman Coulter AU5800 biochemical analysis system with corresponding reagents.

Determination of serum 25-hydroxyvitamin D levels

The serum 25-OH-D levels were measured using the liquid chromatography-tandem mass spectrometry method on the API 4000 liquid chromatography-tandem mass spectrometer (AB SCIEX, USA). All samples were tested strictly following the kit instructions and standard operating procedures.

Statistical analysis

SPSS V.24.0 was used for data entry and statistical analysis in this study. Continuous variables were first examined for normality using the Kolmogorov-Smirnov test alongside visual inspection of histograms and Q-Q plots. Normally distributed continuous variables were statistically described by mean±SD ($\bar{x}\pm s$), and differences between groups were comparatively analysed using the t-test; categorical variables were expressed as n (%), and differences between groups were tested using the χ^2 test, and skewed distributions were described by median (IQR). Differences between groups were tested using the Mann-Whitney U test, due to the large sample size, the statistic U is approximately normally distributed, and the statistic U is converted to a Z value. Confounders were adjusted stepwise, and all independent variables were assessed for collinearity. Variables with a variance inflation factor <2 were retained. Covariates included age, gender, education level, TC, systolic pressure, diastolic pressure, hypertension, heart disease, type 2 diabetes and stroke. Logistic regression was employed to examine the association between serum 25-OH-D levels and MCI. Multiple linear regression was applied to explore the relationship between serum 25-OH-D levels and different dimensions of cognitive function. Subgroup analyses were performed according to age, gender and education level, and the interaction with the multiplication of serum 25-OH-D levels was analysed. Age was categorised into two subgroups: <76 and ≥76 years based on the median age of the sample. In this study, the statistically significant difference was $p<0.05$, and all statistical tests were two-sided to ensure the objectivity and reliability of the results.

RESULTS

Basic characteristics of the study population

A total of 866 participants were enrolled in this study, with a 12.0% prevalence of MCI. Participants had a mean age of 76.72±9.44 years, with 34.2% as male. The majority (60.9%) had a high school and below, while 39.1% had a bachelor's degree and above. The overall serum 25-OH-D level of the study population was 27.76±8.42 ng/mL, ranging from a minimum of 7.35 ng/mL to a maximum of 43.07 ng/mL. The participants were divided into two groups: MCI group and non-MCI group. There was no significant difference in all variables between the MCI and non-MCI groups ($p>0.05$), except for heart disease. Basic characteristics of the study population are summarised in table 1.

Association of serum 25-hydroxyvitamin D levels with mild cognitive impairment

After adjusting for age, gender, education level, TC, systolic pressure, diastolic pressure, hypertension,

Table 1 Basic characteristics of the study population

General characteristics	All	MCI	Non-MCI	Statistical value (t/F/Z)	P value
Number of people	866 (100)	104 (12.0)	762 (88.0)		
Age (years)	76.72±9.44	76.59±9.15	76.74±9.48	0.158*	0.874
Gender					
Man	296 (34.2)	30 (28.8)	266 (34.9)	1.494†	0.222
Woman	570 (65.8)	74 (71.2)	496 (65.1)		
Education level					
Bachelor's degree and above	339 (39.1)	38 (36.5)	302 (39.6)	0.348†	0.555
High school and below	527 (60.9)	66 (63.5)	460 (60.4)		
Systolic pressure	133.00 (122.00, 146.00)	132.00 (121.25, 145.50)	133.00 (122.00, 146.00)	−0.110‡	0.912
Diastolic pressure	74.00 (67.00, 81.00)	74.50 (68.00, 82.75)	74.00 (67.00, 81.00)	−1.009‡	0.313
Total cholesterol (mg/dL)	191.50 (165.00, 218.25)	198.00 (161.75, 217.75)	191.00 (165.00, 219.00)	−0.275‡	0.783
Serum 25-OH-D (ng/mL)	27.76±8.42	15.58±3.51	29.42±7.47	18.602*	<0.01
Hypertension					
Yes	479 (55.3)	58 (55.8)	421 (55.2)	0.010†	0.920
No	387 (44.7)	46 (44.2)	341 (44.8)		
Type 2 diabetes					
Yes	96 (11.1)	11 (10.6)	85 (11.2)	0.031†	0.860
No	770 (88.9)	93 (89.4)	677 (88.8)		
Stroke					
Yes	81 (9.4)	10 (10.0)	72 (9.4)	0.039†	0.844
No	785 (90.6)	94 (90.0)	690 (90.6)		
Heart disease					
Yes	86 (9.9)	17 (16.3)	70 (9.1)	5.436†	0.020§
No	780 (90.1)	87 (83.7)	692 (90.9)		

Normally distributed continuous variables use mean±SD ($\bar{x}$±s); categorical variables use number of cases, constituent ratio n (%); skewed distribution uses median (IQR) M (Q_1, Q_3).
*Indicate T value.
†Indicate F value.
‡Indicate Z value.
§P < 0.05.
25-OH-D, 25-hydroxyvitamin D.

heart disease, type 2 diabetes and stroke, logistic regression analysis showed that higher serum 25-OH-D levels were significantly associated with lower odds of MCI (adjusted OR 0.180, 95% CI 0.105 to 0.306). Detailed results are presented in table 2.

Subgroup analysis of the association between serum 25-hydroxyvitamin D levels and mild cognitive impairment

Participants were categorised into subgroups by average age (<76and ≥76 years), gender and education level (bachelor's degree and above, high school and below). After stepwise adjustment of covariates, the results showed that there were specific associations among subgroups defined by age, gender and education level (p<0.05), and there was no interaction between age, gender, education level and serum 25-OH-D levels (p>0.05), as shown in online supplemental figure 2.

Association of serum 25-hydroxyvitamin D levels with cognitive performance

The association between serum 25-OH-D levels and cognitive performance was analysed by multiple linear regression. Stepwise adjustments were made for age, gender, education level, TC, systolic pressure, diastolic pressure, hypertension, heart disease, type 2 diabetes and stroke. Serum 25-OH-D levels were significantly and positively associated with FIQ (β 0.125, 95% CI 0.026 to 0.224) and VIQ (β 0.120, 95% CI 0.029 to 0.212). There was no significant association between serum 25-OH-D levels and PIQ (p>0.05) as shown in table 3.

Subgroup analysis of the association between serum 25-hydroxyvitamin D levels and cognitive performance

Further subgroup analyses showed that the associations between serum 25-OH-D levels and cognitive function did

Table 2 Association of serum 25-OH-D levels with MCI

	OR (95% CI)	P value
Crude model	0.164 (0.095 to 0.284)	<0.001*
Model 1	0.168 (0.098 to 0.288)	<0.001*
Model 2	0.169 (0.099 to 0.288)	<0.001*
Model 3	0.180 (0.105 to 0.306)	<0.001*

In all logistic regression models, the dichotomous outcome variable was coded as 1 for the MCI group and 0 for the non-MCI group. Model 1: adjusted for age, gender and education level; model 2: further inclusion of TC, systolic pressure and diastolic pressure based on model 1; model 3: further inclusion of hypertension, heart disease, type 2 diabetes and stroke based on model 2.
*p < 0.05.
MCI, mild cognitive impairment; 25-OH-D, 25-hydroxyvitamin D; TC, total cholesterol.

not significantly differ by age, gender or education level, with no statistical evidence of interactive effects. Online supplemental figures 3–5 for details. Specifically, serum 25-OH-D levels were significantly and positively associated with FIQ (β 0.176, 95% CI 0.031 to 0.320) and VIQ (β 0.185, 95% CI 0.050 to 0.321) in the older adults over 76 years, while there was no statistically significant association in the older adults under 76 years. There was a significant association with FIQ (β 0.155,95% CI 0.003 to 0.307) only in males, while there was no statistically significant association in females. There were positive associations with FIQ (β 0.239, 95% CI 0.082 to 0.395) and VIQ (β 0.200, 95% CI 0.057 to 0.334) in the older adults with bachelor's degree and above, while there was no statistically significant association in the older adults with high school and below.

Association between serum 25-hydroxyvitamin D levels and Wechsler Adult Intelligence Scale Revised in China subtest scores

Association between serum 25-hydroxyvitamin D levels and scores on the verbal dimension

After adjusting for the covariates, the results of the multiple linear regression showed that serum 25-OH-D levels were significantly and positively associated with information (β 0.052,95% CI 0.010 to 0.095), similarity (β 0.050,95% CI 0.010 to 0.090) and vocabulary (β 0.144,95% CI 0.034 to 0.253), as shown in table 4.

Association between serum 25-hydroxyvitamin D levels and scores on the performance dimension

After adjusting for the covariates, the results of the multiple linear regression showed that there was no significant association between serum 25-OH-D levels and scores on the performance dimension (p>0.05), as shown in table 5.

DISCUSSION

The results of this cross-sectional study showed that higher serum 25-OH-D levels were significantly associated with lower odds of MCI (p<0.05). Furthermore, there were significant and positive associations between serum 25-OH-D levels and multiple dimensions of cognitive function, specifically FIQ, VIQ and the subdomains of information, similarity and vocabulary (p<0.05).

In the present study, higher serum 25-OH-D levels were significantly associated with lower odds of MCI (p<0.05), consistent with findings from several prior studies exploring this association. Multiple cross-sectional studies have shown that lower levels of serum 25-OH-D were significantly associated with higher risk of MCI.[24 25] While the mechanisms underlying the association between serum 25-OH-D levels and MCI remain incomplete, neuroimaging studies suggest lower levels of serum 25-OH-D are associated with reduced hippocampal volume and disrupted structural connectivity in patients with MCI.[26] Furthermore, emerging evidence suggests that vitamin D influences cognitive function through multiple pathways, which include antioxidant effects,[27] inhibition of inflammatory responses,[15 28] promotion of neurotrophic factor synthesis,[29] modulation of intracellular calcium homeostasis in neuronal cells[30] and inhibition of β-amyloid (Aβ) deposition,[31] among other pathways.

The study further explored the associations between serum 25-OH-D levels and different dimensions of cognitive function. The results showed that serum 25-OH-D levels were significantly and positively associated with FIQ and VIQ (p<0.05). These findings align with prior research showing significant associations between serum 25-OH-D levels and

Table 3 Association of serum 25-OH-D levels with cognitive performance

	FIQ		VIQ		PIQ	
	β (95% CI)	P value	β (95% CI)	P value	β (95% CI)	P value
Crude model	0.111 (0.016 to 0.206)	0.022*	0.104 (0.016 to 0.191)	0.020*	−0.001 (−0.105 to 0.102)	0.983
Model 1	0.112 (0.017 to 0.207)	0.021*	0.105 (0.018 to 0.193)	0.019*	−0.002 (−0.105 to 0.102)	0.975
Model 2	0.015 (0.022 to 0.208)	0.016*	0.108 (0.022 to 0.195)	0.014*	0.003 (−0.098 to 0.104)	0.953
Model 3	0.125 (0.026 to 0.224)	0.014*	0.120 (0.029 to 0.212)	0.010*	0.018 (−0.090 to 0.125)	0.749

Model 1: adjusted for age, gender and education level; model 2: further inclusion of TC and systolic pressure, diastolic pressure based on model 1; model 3: further inclusion of hypertension, heart disease, type 2 diabetes, stroke based on model 2.
*p<0.05.
FIQ, full IQ; 25-OH-D, 25-hydroxyvitamin D; PIQ, performance IQ; TC, total cholesterol; VIQ, verbal IQ.

Table 4 Association between serum 25-OH-D levels and scores on the verbal dimension

	Crude model		Model 1		Model 2		Model 3	
	β (95% CI)	P value	β (95% CI)	P value	β (95% CI)	P value	β (95% CI)	P value
Information	0.046 (0.005 to 0.087)	0.027*	0.047 (0.006 to 0.088)	0.024*	0.049 (0.009 to 0.089)	0.017*	0.052 (0.010 to 0.095)	0.016*
Comprehension	0.023 (–0.017 to 0.064)	0.258	0.024 (–0.016 to 0.065)	0.239	0.026 (–0.014 to 0.066)	0.201	0.028 (–0.015 to 0.071)	0.198
Arithmetic	0.004 (–0.007 to 0.015)	0.485	0.004 (–0.007 to 0.015)	0.484	0.004 (–0.007 to 0.015)	0.494	0.006 (–0.006 to 0.018)	0.353
Similarity	0.043 (0.006 to 0.081)	0.024*	0.043 (0.005 to 0.081)	0.025*	0.044 (0.007 to 0.081)	0.021*	0.050 (0.010 to 0.090)	0.014*
Digit span	0.009 (–0.019 to 0.038)	0.510	0.009 (–0.019 to 0.038)	0.518	0.010 (–0.019 to 0.038)	0.505	0.021 (–0.009 to 0.052)	0.172
Vocabulary	0.138 (0.034 to 0.242)	0.009*	0.142 (0.038 to 0.245)	0.008*	0.144 (0.041 to 0.248)	0.006*	0.144 (0.034 to 0.253)	0.010*

Model 1: adjusted for age, gender and education level; model 2: further inclusion of TC, systolic pressure and diastolic pressure based on model 1; model 3: further inclusion of hypertension, heart disease, type 2 diabetes and stroke based on model 2.
*p<0.05.
25-OH-D, 25-hydroxyvitamin D; TC, total cholesterol.

Table 5 Association between serum 25-OH-D levels and scores on the performance dimension

	Crude model		Model 1		Model 2		Model 3	
	β (95% CI)	P value	β (95% CI)	P value	β (95% CI)	P value	β (95% CI)	P value
Digital symbol	0.048 (–0.027 to 0.124)	0.208	0.050 (–0.025 to 0.125)	0.194	0.054 (–0.021 to 0.128)	0.157	0.056 (–0.024 to 0.135)	0.168
Picture completion	–0.009 (–0.045 to 0.027)	0.631	–0.009 (–0.045 to 0.027)	0.624	–0.008 (–0.044 to 0.027)	0.651	–0.014 (–0.052 to 0.024)	0.476
Block design	0.012 (–0.045 to 0.070)	0.672	0.012 (–0.046 to 0.070)	0.684	0.014 (–0.043 to 0.070)	0.637	0.025 (–0.036 to 0.087)	0.419
Object assembly	–0.015 (–0.073 to 0.043)	0.608	–0.015 (–0.073 to 0.043)	0.609	–0.013 (–0.071 to 0.044)	0.652	0.004 (–0.058 to 0.065)	0.910
Picture arrangement	–0.001 (–0.063 to 0.060)	0.965	–0.003 (–0.064 to 0.059)	0.935	–0.001 (–0.061 to 0.060)	0.983	0.014 (–0.051 to 0.078)	0.678

Model 1: adjusted for age, gender and education level; model 2: further inclusion of TC, systolic pressure and diastolic pressure based on model 1; model 3: further inclusion of hypertension, heart disease, type 2 diabetes and stroke based on model 2.
25-OH-D, 25-hydroxyvitamin D; TC, total cholesterol.

cognitive function. Serum 25-OH-D plays diverse roles in brain development and function.[32 33] Specifically, these prior studies used comprehensive neuropsychological batteries to differentiate between distinct cognitive domains; they observed that higher serum 25-OH-D levels were predominantly linked to superior verbal ability, memory and global cognition. Mechanistically, lower serum 25-OH-D levels may contribute to brain structural and functional impairment, a study has shown a significant association between 25-OH-D levels and brain volume, as well as white matter integrity in urban adults.[34] Lower serum 25-OH-D levels lead to a decrease in the level of dopamine, accumulation of synuclein and demyelination of neurons.[35]

Interestingly, serum 25-OH-D levels were significantly associated with VIQ but not PIQ. This divergence may stem from domain-specific sensitivities and unique measurement characteristics. Verbal subtests primarily reflect 'crystallised intelligence', which might be more receptive to the long-term neuroprotective benefits of vitamin D. Conversely, performance subtests capture 'fluid intelligence'; these non-verbal tasks are highly vulnerable to age-related motor or visual slowing during testing, which could confound the results and potentially mask the subtle effects of vitamin D.[36] Additionally, since multiple cognitive domains were evaluated simultaneously, the possibility of chance findings due to multiple comparisons cannot be entirely ruled out.[37] These domain-specific patterns require further verification in future longitudinal studies.

The results also showed that serum 25-OH-D levels were significantly and positively associated with three dimensions: information, similarity and vocabulary ($p<0.05$). The information dimension reflects the breadth of knowledge, memory ability. From a neurological point of view, vitamin D receptors are expressed in the frontal and parietal cortices of the cerebral cortex, regions critical for memory.[38] Vitamin D enhances hippocampal function, mitigates cognitive deficits and improves memory;[39] the similarity dimension assesses logical reasoning, abstract thinking and summarising abilities. Serum 25-OH-D levels are closely related to the development and volume of the hippocampus.[40] The hippocampus also has an important role in logical reasoning and abstract thinking.[41] The vocabulary dimension measures sensitivity to new expertise and storage and reorganisation capabilities. A study found an association between cortical surface area in the left posterior-inferior precuneus and vocabulary learning aptitude.[42] Higher serum 25-OH-D levels are protective against cortical atrophy.[43]

Furthermore, subgroup analyses demonstrated that the associations between serum 25-OH-D levels and cognitive function did not significantly differ by age, gender or education level. This indicates that the associations between vitamin D and cognitive function are robust and consistent across these different demographic strata, with no statistical evidence of interactive effects.

However, due to the cross-sectional design of this study, the risk of reverse causality cannot be overlooked. It is highly plausible that individuals with MCI may experience a decline in daily functioning, leading to a reduction in outdoor activities, less sun exposure and a deterioration in dietary quality. These lifestyle modifications driven by early cognitive decline could subsequently result in a secondary decrease in serum 25-OH-D levels. Therefore, prospective longitudinal studies are warranted to untangle this directional relationship.

CONCLUSION

Higher serum 25-OH-D levels were significantly associated with lower odds of MCI, as well as with MCI across all subgroups ($p<0.05$). Furthermore, there were significant and positive associations between serum 25-OH-D levels and multiple dimensions of cognitive function, specifically FIQ, VIQ and the subdomains of information, similarity and vocabulary.

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Acknowledgements We are grateful to all participants who took part in this study, the staff at the research centre and the data management team for their invaluable efforts in contributing to the study during all these years.

Contributors ZL and XH designed and conceptualised the present study. XW and KD curated the data. ZL and XH conducted the formal analysis and drafted the initial manuscript. XC, LZ, LL, and FM were involved in providing resources and supervision/oversight. FM was involved in funding acquisition. All authors reviewed and substantially revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work. Guarantor: FM.

Funding This work was supported by the National Natural Science Foundation of China Grant [Grant number 82373573].

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Consent obtained directly from patient(s).

Ethics approval This study involves human participants. The ethics application for collecting data on human subjects was approved by the Ethics Committee of Tianjin Medical University (Approval No. TMUh MEC2016031); the research strictly adhered to the principles of the Declaration of Helsinki and participants provided written informed consent. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The dataset generated and analysed during the current study will be available from the corresponding author on a reasonable request.

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