Clinical Interventions in Aging

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Development and Validation of a Predictive Model for Mild Cognitive Impairment in Older Adults with Multimorbidity

Lili Shao[1], Ruyi Zhang[2], Yinqing Huang[2], Xiaochun Dai[3]

[1]Department of Geriatric Medicine, The Affiliated Kangning Hospital of Wenzhou Medical University, Zhejiang Provincial Clinical Research Center for Mental Disorder, Wenzhou, Zhejiang, 325000, People's Republic of China; [2]Department of Geriatric Medicine, The Affiliated Kangning Hospital of Wenzhou Medical University, Wenzhou, Zhejiang, 325000, People's Republic of China; [3]Department of Medicine, The Affiliated Kangning Hospital of Wenzhou Medical University, Zhejiang Provincial Clinical Research Center for Mental Disorder, Wenzhou, Zhejiang, 325000, People's Republic of China

Correspondence: Xiaochun Dai, Department of Medicine, The Affiliated Kangning Hospital of Wenzhou Medical University, Zhejiang Provincial Clinical Research Center for Mental Disorder, No. 1, Shengjin Road, Huanglong Residential Quarter, Wenzhou, Zhejiang, 325000, People's Republic of China, Email epw6492@163.com

Objective: To identify factors associated with mild cognitive impairment (MCI) in older adults with multimorbidity and to develop and validate a predictive model for early screening.

Methods: This cross-sectional study consecutively enrolled 238 older adult inpatients with multimorbidity at the Affiliated Kangning Hospital of Wenzhou Medical University, China, between April 2022 and February 2025. Participants were assessed using a self-designed general information questionnaire and the Montreal Cognitive Assessment Basic Scale (MoCA-B). MCI was diagnosed according to the Chinese Expert Consensus. Associated factors were identified using logistic regression analysis. A nomogram prediction model was constructed based on these factors. The model's performance was evaluated using the receiver operating characteristic (ROC) curve, calibration curve, and decision curve analysis (DCA). An external validation cohort (n=68) was used to further test the model.

Results: MCI prevalence was 26.81%. Risk factors: age ≥80 years (OR=3.23), hearing impairment (OR=4.04), and emotional disorders (OR=3.25). Protective factors: higher education (OR=0.23), more frequent physical exercise (OR=0.15), and more frequent social activities (OR=0.26) (all P<0.05). The AUC was 0.862 (training) and 0.832 (external validation). Calibration curves showed good agreement, and DCA indicated net clinical benefit across threshold probabilities of (10–65%).

Conclusion: Age, hearing impairment, emotional disorders, education, physical exercise, and social activities are significantly associated with MCI in older adults with multimorbidity. The nomogram demonstrates good predictive accuracy and clinical utility, aiding early identification and targeted prevention.

Keywords: multimorbidity, elderly, mild cognitive impairment, prediction model, prevention and control measures, predictive performance

Introduction

According to data from the National Bureau of Statistics, China's population aged 60 and above reached 310 million in 2024, and the population aged 80 is projected to reach 100 million by 2050, with an ageing rate twice the global average.[1] Against this backdrop of rapid population ageing, the prevalence of multimorbidity remains high. Surveys indicate that the incidence of multimorbidity among hospitalised older adults reaches 91.16%, with an average of 4.68 coexisting conditions per individual.[2]

Compared with single chronic diseases, multimorbidity not only increases the complexity of diagnosis and treatment but also leads to progressive depletion of physiological function and a decline in quality of life among older adults. It can further trigger a cascade of adverse outcomes, including physical frailty, cognitive decline, disability, and even mortality.

https://doi.org/10.2147/CIA.S608488
Received: 16 March 2026
Accepted: 23 June 2026
Published: 21 July 2026

Mild cognitive impairment (MCI) represents the prodromal stage of Alzheimer's disease and other dementia.[3,4] It not only increases the risk of dementia but is also closely associated with higher levels of functional dependence, reduced quality of life, and greater caregiving burden among older adults. Multimorbidity constitutes a high-risk factor for MCI.[5]

Early identification of MCI in this population is therefore crucial for implementing targeted interventions and delaying the onset of dementia. Although previous domestic and international studies have analysed risk factors for MCI in older adults, most have focused on single chronic conditions such as type 2 diabetes, hypertension, or heart failure, overlooking the complexity inherent to multimorbidity.[6,7] Furthermore, clinical practice currently lacks systematic research and predictive tools specifically designed to assess MCI risk in older adults with multimorbidity, limiting the ability to identify high-risk individuals at an early stage and resulting in delayed interventions.

Despite the above-mentioned evidence, a clear scientific gap remains: few studies have specifically focused on MCI prediction in older adults with multimorbidity, and existing predictive tools are often limited by complex assessments, lack of external validation, or poor applicability in routine clinical practice. To address this gap, the present study focuses on older adults with multimorbidity. We hypothesized that a combination of sociodemographic, sensory, psychological, and lifestyle factors would be significantly associated with MCI, and that a nomogram constructed from these factors would demonstrate good discriminative ability and clinical utility. Compared with existing approaches, our nomogram offers added value by using only routinely available clinical variables (age, education, hearing, emotional status, physical exercise, and social activities), thereby eliminating the need for specialized equipment or lengthy neuropsychological testing. Using logistic regression for variable selection, a nomogram was developed. The advantage of this model lies in its ability to translate complex statistical findings into a visual and practical tool. This enables healthcare professionals to integrate multiple factors efficiently and rapidly assess an individual's risk of developing MCI at the point of care without relying on computerized calculations. This visual tool can assist providers in identifying high-risk individuals who would benefit from formal cognitive screening and closer clinical follow-up, thereby informing early prevention strategies and promoting healthy ageing.

Materials and Methods

Study Population

This cross-sectional study prospectively enrolled a total of 238 older adults with multimorbidity admitted to the Affiliated Kangning Hospital of Wenzhou Medical University from April 2022 to February 2025. The sample size was determined following the recommendations by Riley et al for developing clinical prediction models.[8] Based on an anticipated MCI incidence of 28.36% among older adults with multimorbidity[9], a target Cox-Snell R^2 of 0.15, and a final model including 6 predictor parameters, a minimum of 200 participants was required to achieve a shrinkage factor of 0.90 and minimize overfitting. Allowing for 10% invalid responses, we aimed to recruit at least 220 participants. The final sample of 235 participants exceeded this target, ensuring sufficient statistical power for model development and internal validation.

Assessment Tools

General Data Questionnaire

Key variables from existing MCI assessment tools were reviewed, and a general data questionnaire was developed following expert consultation. It included gender, age, objectively measured body mass index, education level, monthly household income, living arrangements, smoking history, alcohol consumption, hearing impairment, and number of comorbidities.

Physical exercise frequency was assessed by asking participants: "How often have you engaged in any physical activity lasting at least 30 minutes in the past six months?" Response options were: none (<1 time/week), occasional (1–2 times/week), and regular (3–5 times/week). The type of exercise (walking, jogging) was recorded but not included in the final model due to small subsample sizes. No standardized questionnaire (IPAQ) was used, as the study aimed for a brief clinical screening tool.

Social activity frequency was assessed using a similar single item: "How often do you participate in social activities (community gatherings, mahjong, chatting with friends)?" with the same three frequency categories.

Emotional disorders were assessed using the Chinese version of the Hospital Anxiety and Depression Scale (HADS). A subscale score ≥8 for anxiety or depression was defined as clinically significant emotional disorder. When the HADS was not administered (eg, due to time constraints), documented clinical diagnosis of major depressive disorder or generalized anxiety disorder in the electronic medical record was used.

The number of comorbidities and types of medications were objectively ascertained through review of the patients' electronic medical records. All predictors were collected prior to the cognitive assessment to ensure temporal relevance for prediction.

Montreal Cognitive Assessment Basic Version (MoCA-B)

The scale assesses six cognitive domains with 12 core items, yielding a total score of 30. Administration takes approximately 10–15 minutes, with higher scores indicating better cognitive function. MCI screening cut-off scores are: >12 years of education, 24 points; 7–12 years, 22 points; ≤6 years, 19 points. The scale demonstrated good reliability and validity, with a Cronbach's α of 0.812, test–retest reliability of 0.943, and content validity of 0.910. The researchers conducting the MoCA-B assessments were blinded to the participants' other clinical and demographic information (eg, age, hearing status, emotional disorders) to minimize assessment bias.[10]

MCI Assessment and Grouping

MCI was diagnosed according to the criteria in the *Chinese Expert Consensus on the Diagnosis and Treatment of Alzheimer's Disease–Related Mild Cognitive Impairment*,[11] requiring the presence of the following: (1) Cognitive impairment reported by the patient or an informant, or identified by a clinician; (2) Objective evidence of impairment in at least one cognitive domain; (3) Complex instrumental activities of daily living (IADLs) were assessed using the Lawton IADL Scale and were defined as slightly impaired if the participant required assistance or reported difficulties in at least one domain, such as managing finances, medication, or transportation, while basic activities of daily living assessed by the Barthel Index remained independent (score = 100).

Data Collection and Quality Control

All investigators received standardized training and participated in the survey only after passing assessment. Unified instructions were given to explain the questionnaire and scale procedures. Participants completed the paper questionnaires independently once they understood the instructions. For those unable to complete the forms themselves, investigators read the questions aloud and patiently explained the content, recording responses on behalf of the participant. On-site supervision ensured adherence to procedures. Completed questionnaires were immediately reviewed; missing items were verified and completed with the participant. Questionnaires with more than 20% missing items were excluded. Information on all predictors was collected prior to the cognitive assessment to ensure temporal relevance for prediction. Regarding missing data, items in the general questionnaire were verified on-site to minimize omissions. For the few variables with missing values (constituting less than 2% of the total data), a complete-case analysis was applied as the primary approach, given the low missing rate and its random nature.

Nomogram Development and Validation

The final logistic regression model was presented as a nomogram using the rms package in R (version 4.3.1) to provide a visual tool for clinical risk prediction. The nomogram assigns points for each predictor by scaling its regression coefficient, allowing the summation of these points to derive a total score. This total score is then converted into a predicted probability of MCI based on the underlying logistic regression equation. Model calibration was evaluated using calibration curves with bootstrapping (1000 resamples). For clinical application, the nomogram is designed as a printable chart for rapid assessment, with plans for future development of an online calculator to enhance accessibility.

External Validation

To provide an initial test of the model's generalizability beyond the specific patient population of the development cohort, an external validation cohort was prospectively enrolled from a different clinical department (the Department of Neurology)

within The First Affiliated Hospital of Xiamen University between March and June 2024. The recruitment strategy and eligibility criteria were identical to those used for the development cohort. Data collection followed the same standardized protocol, utilizing the same general data questionnaire and MoCA-B assessment under identical quality control procedures, to ensure consistency while testing performance in a distinct clinical setting within the same institution.

Statistical Analysis

Data were analysed using SPSS 27.0. Categorical variables are expressed as n (%), compared using the χ^2-test. Ordinal data were analysed with the rank-sum test. Variable selection for the multivariable logistic regression model was performed as follows: based on a priori clinical knowledge and methodological guidelines, sex was pre-specified and forced into the model. In addition, all other variables that showed statistical significance ($P < 0.05$) in the univariate analysis were entered using the enter method. This logistic regression identified factors influencing MCI. An MCI risk prediction model and nomogram were constructed in R software. Receiver operating characteristic (ROC) curves assessed model discrimination, with the area under the curve (AUC) closer to 1 indicating better discrimination. Calibration curves evaluated model calibration. Decision curve analysis (DCA) assessed clinical benefit; a higher net benefit above the None and All lines indicated greater clinical utility. Significance level was set at $\alpha = 0.05$. The final prediction model is presented as a nomogram for clinical use. The complete model equation, including all coefficients and the intercept. Internal Validation: To quantify and adjust for the model's optimism, we performed internal validation using bootstrap resampling with 1000 replicates on the development cohort. This provided a bias-corrected (optimism-corrected) estimate of the model's discrimination (C-statistic) and calibration.

Results

Cognitive Function and MCI Incidence in Older Adults with Multimorbidity

A total of 238 questionnaires were distributed, of which 2 incomplete and 1 patterned-response questionnaires were excluded, yielding 235 valid responses and an effective response rate of 98.74%. Among these 235 participants, the incidence of MCI was 26.81% (63/235), with MoCA-B scores ranging from 14 to 30 (23.69 ± 3.10).

Univariate and Multivariate Logistic Regression Analysis of MCI

Comparisons between the MCI and non-MCI groups showed significant differences in age, education level, frequency of physical exercise, frequency of social activities, hearing impairment, and emotional disorders ($P < 0.05$). No significant differences were found for monthly household income, living arrangements, smoking history, gender, alcohol consumption, number of comorbidities, body mass index, or medication types ($P > 0.05$), as shown in Table 1.

Variables with significance were entered sequentially into the logistic regression model using the entry method; coding is shown in Table 2. Results indicated that age, hearing impairment, and emotional disorders were independent risk factors for MCI in older adults with multimorbidity, while education level, frequency of physical exercise, and frequency of social activities were protective factors ($P < 0.05$). Sex was included in the model as a pre-specified variable but was not independently associated with MCI in this cohort (OR=1.21, 95% CI: 0.65–2.28, P=0.548), as shown in Table 3.

Nomogram for Predicting MCI Risk in Older Adults with Multimorbidity

A nomogram was constructed to predict MCI risk in older adults with multimorbidity, with age, hearing impairment, emotional disorders, education level, frequency of physical exercise, and frequency of social activities as independent variables, and MCI occurrence as the dependent variable. The total score ranges from 0 to 500, corresponding to an MCI risk of 1%–99% (Figure 1).

Validation of the MCI Risk Prediction Model in Older Adults with Multimorbidity

A total of 68 older adults with multimorbidity admitted to the Affiliated Kangning Hospital of Wenzhou Medical University from March to June 2025 were selected as the validation cohort, including 37 men and 31 women, with a mean age of 71.35 ± 4.69 years and a mean body mass index of 22.32 ± 1.10 kg/m^2.

Table 1 Comparison of MCI Distribution Among Older Adults with Multimorbidity by Different Characteristics

Items	MCI Group (n = 63)		Non-MCI Group (n = 172)		Z/χ^2 value	P value
	Number of cases	Rate	Number of cases	Rate		
Sex					0.170	0.681
Male	34	53.97	98	56.98		
Female	29	46.03	74	43.02		
Age					12.875	<0.001
< 80 years	25	39.68	113	65.70		
≥ 80 years	38	60.32	59	34.30		
Body Mass Index					0.646	0.889
< 18.5 kg/m^2	15	23.81	45	26.16		
18.5–23.9 kg/m^2	35	55.56	97	56.40		
24.0–27.9 kg/m^2	9	14.29	23	13.37		
≥ 28 kg/m^2	4	6.35	7	4.07		
Education Level					2.601	0.009
Primary school or below	42	66.67	85	49.42		
Junior high school	12	19.05	28	16.28		
Senior high school/vocational school	7	11.11	38	22.09		
College or above	2	3.17	21	12.21		
Monthly Household Income					0.652	0.419
< 3000 RMB	47	74.60	119	69.19		
≥ 3000 RMB	16	25.40	53	30.81		
Living Arrangement					0.466	0.495
Living alone	11	17.46	37	21.51		
Living with family	52	82.54	135	78.49		
Smoking History					0.136	0.712
Yes	18	28.57	45	26.16		
No	45	71.43	127	73.84		
Alcohol Consumption					0.191	0.662
Yes	16	25.40	39	22.67		
No	47	74.60	133	77.33		
Frequency of Physical Exercise					20.329	<0.001
None	30	47.62	35	20.35		
Occasional	10	15.87	68	39.53		
Regular	23	36.51	69	40.12		
Frequency of Social Activities					16.362	<0.001
None	31	49.21	43	25.00		
Occasional	22	34.92	61	35.47		
Regular	10	15.87	68	39.53		
Hearing Impairment					13.644	<0.001
Yes	28	44.44	35	20.35		
No	35	55.56	137	79.65		
Emotional Disorders					11.904	<0.001
Yes	24	38.10	29	16.86		
No	39	61.90	143	83.14		
Number of Comorbidities					0.290	0.590
2	39	61.90	113	65.70		
≥ 3	24	38.10	59	34.30		
Number of Medications					3.170	0.205
2	18	28.57	58	33.72		
3	32	50.79	94	54.65		
≥ 4	13	20.63	20	11.63		

Notes: Data are presented as n (%). MCI: Mild Cognitive Impairment. Categorical variables were compared using the Chi-square (χ^2) test. P values < 0.05 were considered statistically significant and are highlighted in bold.

https://doi.org/10.2147/CIA.S608488

Table 2 Variable Coding Table

Variable	Coding Method
Dependent Variable	
MCI	No = 0, Yes = 1
Independent Variables	
Age	<80 years = 1, ≥80 years = 2
Hearing impairment	No = 0, Yes = 1
Emotional disorders	No = 0, Yes = 1
Education level	Primary school or below = 1, Junior high school = 2, Senior high school/technical secondary school = 3, College degree or above = 4
Frequency of physical exercise	No exercise = 1, Occasional = 2, Regular = 3
Frequency of social activities	No participation = 1, Occasional = 2, Regular = 3

Table 3 Logistic Regression Analysis

Variable	*β*	*S.E.*	*Wald*χ^2	*OR*	*95% CI*		*P*
					Lower Limit	Upper Limit	
Sex	0.190	0.316	0.362	1.210	0.650	2.280	0.548
Age	1.172	0.369	10.093	3.227	1.572	6.653	0.001
Hearing impairment	1.394	0.381	13.410	4.035	1.912	8.564	<0.001
Emotional disorders	1.179	0.407	8.404	3.250	1.465	7.216	0.004
Education level	−1.452	0.298	23.743	0.234	0.131	0.420	<0.001
Frequency of physical exercise	−1.932	0.500	14.954	0.145	0.057	0.394	<0.001
Frequency of social activities	−1.336	0.494	7.322	0.263	0.103	0.697	0.007

ROC curves were plotted to assess model performance. The area under the curve (AUC) was 0.862 (95% CI: 0.800–0.942) in the training set and 0.832 (95% CI: 0.775–0.890) in the validation set (Figure 2). Calibration plots showed high agreement between predicted and observed MCI risk. The Dxy values for the training and validation sets were 0.665 and 0.724, respectively, indicating a strong correlation between predicted and actual values. The C-statistics (ROC) were 0.832 and 0.862, both close to 1, demonstrating good discriminative ability (Figure 3).

Decision curve analysis (DCA) demonstrated that the "Model" line lay above the "Treat All" and "Treat None" lines across most threshold probabilities. (Figure 4).

Comparison of Development and External Validation Cohorts

The baseline characteristics of the development and external validation cohorts are presented in Table 4. The two cohorts were comparable in terms of key demographic and clinical features.

Internal and Temporal Validation of the Prediction Model

The model's performance was assessed through bootstrap internal validation and an independent temporal validation cohort. Key metrics are summarized in Table 5. The optimism-corrected C-statistic from bootstrap validation was 0.851. In the temporal validation cohort (n=68, 18 events), the model yielded a C-statistic of 0.832 (95% CI: 0.775–0.890), a calibration slope of 0.920, and a Brier score of 0.121.

Discussion

With the ongoing acceleration of population ageing, maintaining the health of older adults and improving their quality of life in later years has become a major global public health challenge.[12] Among various health issues affecting older

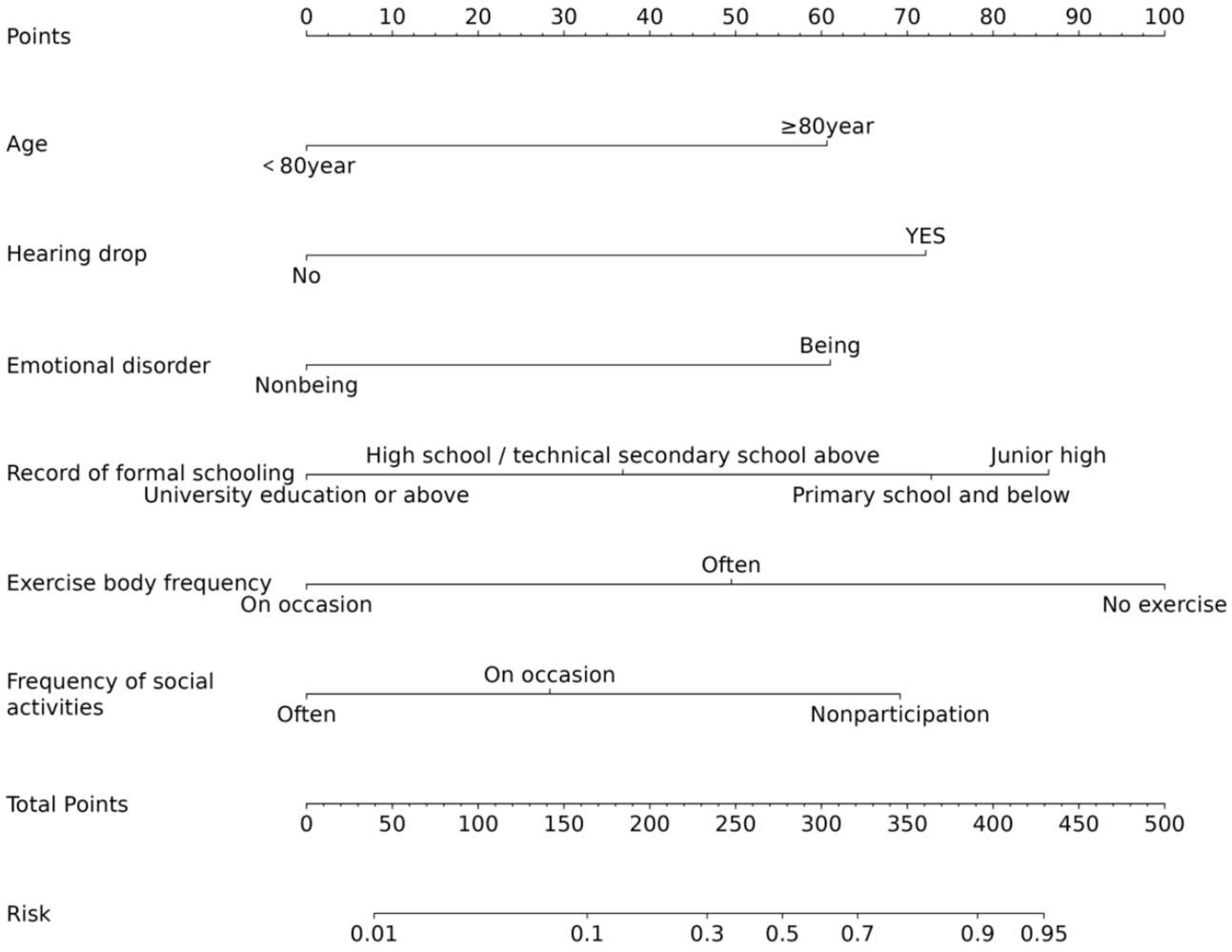

Figure 1 Nomogram for Predicting MCI Risk in Older Adults with Multimorbidity. To use the nomogram, locate the patient's value for each predictor (Age, Hearing Impairment, Emotional Disorders, Education Level, Frequency of Physical Exercise, Frequency of Social Activities) on the corresponding axis, and draw a line upward to the "Points" axis to get the score. Sum all six scores to obtain the "Total Points". The predicted probability of MCI is found by drawing a line down from the "Total Points" axis to the "Risk of MCI" axis.

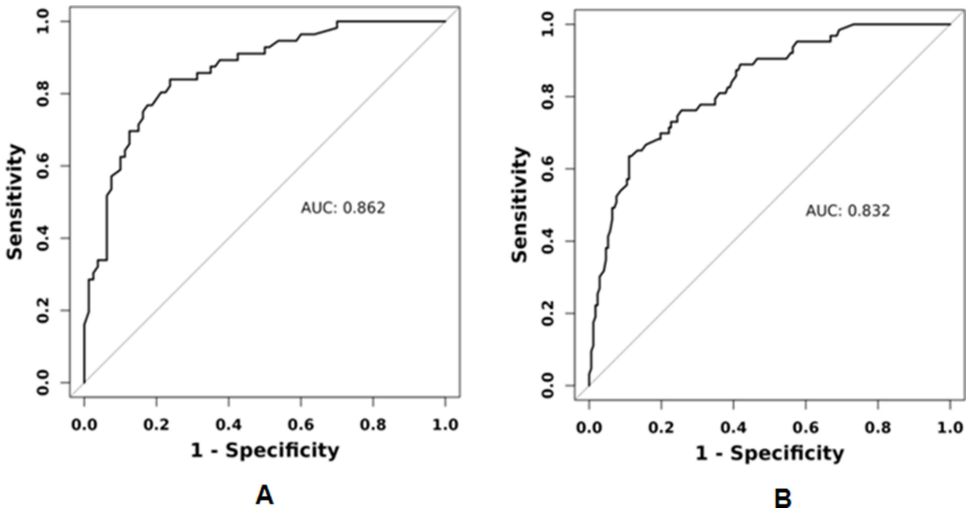

Figure 2 ROC Curve of the Predictive Model. (**A**) ROC Curve in the Training Cohort (n=235). The Area Under the Curve (AUC) was 0.862 (95% CI: 0.800–0.942), indicating excellent discriminatory ability of the model in the development dataset. (**B**) ROC Curve in the External Validation Cohort (n=68). The AUC was 0.832 (95% CI: 0.775–0.890), demonstrating good generalizability and maintained performance in an independent patient sample.

https://doi.org/10.2147/CIA.S608488

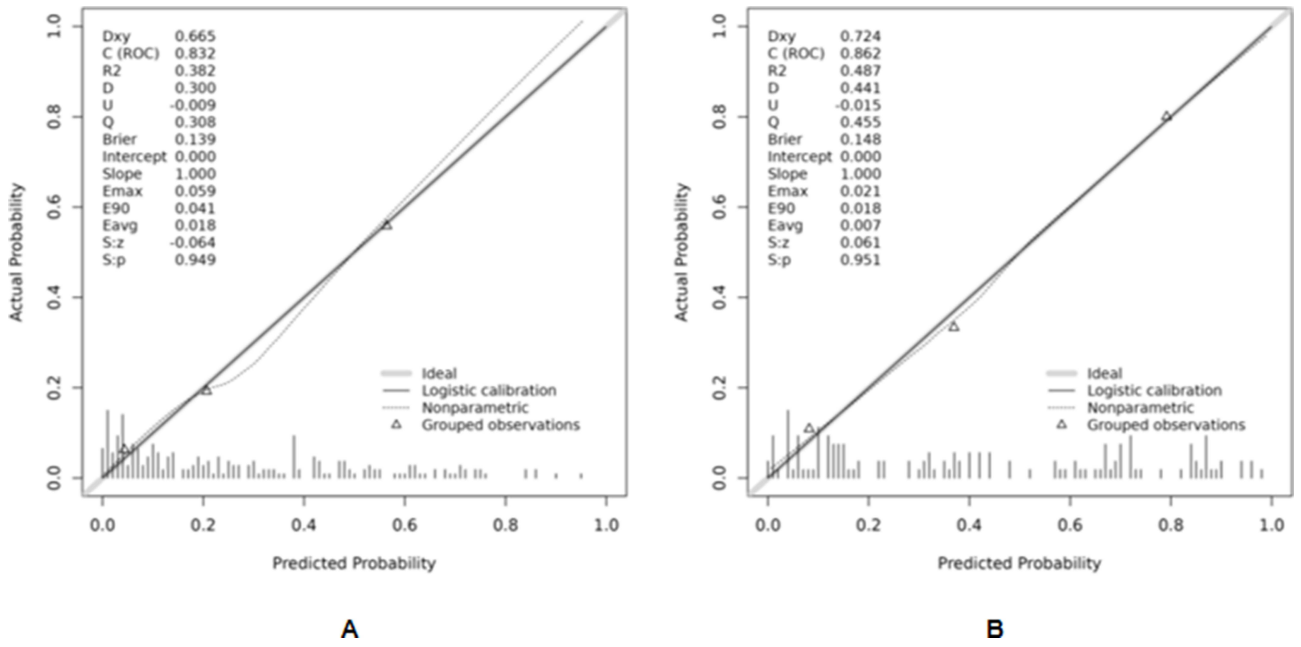

Figure 3 Calibration Curves of the Predictive Model. (**A**) Calibration Curve in the Training Cohort. The solid line represents the apparent accuracy of the model, while the dashed line represents the bias-corrected accuracy after bootstrap validation (1000 resamples). The close alignment of the solid line to the ideal 45-degree diagonal (dotted line) indicates good agreement between predicted probabilities and observed outcomes. (**B**) Calibration Curve in the External Validation Cohort. The plot shows the relationship between predicted risk and actual observed frequency of MCI in the validation set. The model demonstrates satisfactory calibration in the external cohort.

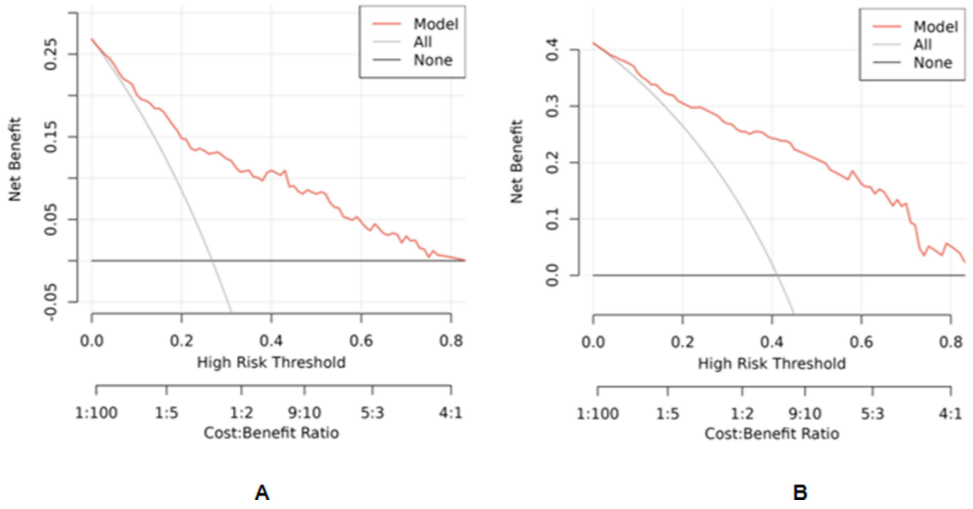

Figure 4 Decision Curve Analysis (DCA) of the Predictive Model. (**A**) (Left): DCA in the Training Cohort. The y-axis represents the net benefit. The red line "Model" shows the net benefit of using the nomogram for clinical decision-making across different threshold probabilities (x-axis). The grey line "None" assumes no patients have MCI, and the black line "All" assumes all patients have MCI. The "Model" curve lies above both the "None" and "All" lines across a wide range of thresholds, indicating that using this model for MCI risk stratification adds clinical net benefit compared to intervening on all or no patients. (**B**) (Right): DCA in the External Validation Cohort. The net benefit of the model was confirmed in the independent validation set, supporting its potential clinical utility.

adults, cognitive decline is particularly prominent. In this study, the incidence of MCI among 235 older adults with multimorbidity was 26.81%, slightly higher than the 25.43% reported by Liu Yalin et al[13] in an older population from a district in Shanghai. This difference is likely attributable to the present study's specific focus on individuals with multimorbidity, a group known to be at elevated risk for cognitive decline, thereby underscoring the importance of targeted investigation in this population.

This study identified several factors significantly associated with MCI in older adults with multimorbidity. Specifically, age ≥80 years, hearing impairment, and emotional disorders were associated with increased odds of MCI,

Table 4 Baseline Characteristics of the Development and External Validation Cohorts

Characteristic	Development Cohort (n=238)	Validation Cohort (n=68)	*P*
Age, n (%)			0.451
< 80 years	138 (58.0%)	43 (63.2%)	
≥ 80 years	100 (42.0%)	25 (36.8%)	
Gender, n (%)			0.682
Male	132 (55.5%)	37 (54.4%)	
Female	106 (44.5%)	31 (45.6%)	
Education Level, n (%)			0.289
Primary school or below	127 (53.4%)	32 (47.1%)	
Junior high school	40 (16.8%)	14 (20.6%)	
Senior high school/vocational school	45 (18.9%)	16 (23.5%)	
College or above	26 (10.9%)	6 (8.8%)	
Monthly Household Income < 3000 RMB, n (%)	166 (69.7%)	44 (64.7%)	0.423
Living Alone, n (%)	48 (20.2%)	11 (16.2%)	0.460
Smoking History, n (%)	63 (26.5%)	16 (23.5%)	0.625
Alcohol Consumption, n (%)	55 (23.1%)	14 (20.6%)	0.664
Frequency of Physical Exercise, n (%)			0.543
None	65 (27.3%)	22 (32.4%)	
Occasional	78 (32.8%)	22 (32.4%)	
Regular	95 (39.9%)	24 (35.3%)	
Frequency of Social Activities, n (%)			0.610
None	74 (31.1%)	24 (35.3%)	
Occasional	83 (34.9%)	21 (30.9%)	
Regular	81 (34.0%)	23 (33.8%)	
Hearing Impairment, n (%)	63 (26.5%)	15 (22.1%)	0.461
Emotional Disorders, n (%)	53 (22.3%)	12 (17.6%)	0.404
Number of Comorbidities, n (%)			0.887
2	152 (63.9%)	44 (64.7%)	
≥ 3	86 (36.1%)	24 (35.3%)	
Body Mass Index, n (%)			0.942
< 18.5 kg/m^2	60 (25.2%)	16 (23.5%)	< 18.5 kg/m^2
18.5–23.9 kg/m^2	132 (55.5%)	39 (57.4%)	18.5–23.9 kg/m^2
24.0–27.9 kg/m^2	32 (13.4%)	9 (13.2%)	24.0–27.9 kg/m^2
≥ 28 kg/m^2	14 (5.9%)	4 (5.9%)	≥ 28 kg/m^2

Table 5 Model Performance in Development and Validation Cohorts

Metric	Development Cohort (Apparent)	Development Cohort (Bootstrap-Corrected)	Temporal Validation Cohort
n (Events)	238 (63)	238 (63)	68 (18)
C-statistic	0.862	0.851	0.832
95% CI	0.800–0.942	-	0.775–0.890
Calibration Slope	1.000	0.950	0.920
Brier Score	0.112	0.115	0.121

whereas higher education level, more frequent physical exercise, and more frequent social activities were associated with decreased odds.

Crucially, due to the cross-sectional nature of this study, these findings represent statistical associations and cannot establish causality or determine the direction of these relationships. For instance, while hearing impairment might

contribute to cognitive load and social isolation leading to MCI, it is also plausible that incipient cognitive decline could affect auditory processing or self-reporting of hearing ability. Similarly, the relationship between emotional disorders and MCI is likely complex and bidirectional. Therefore, these results should be interpreted as identifying factors that co-occur with MCI in this population, generating hypotheses for future longitudinal research to explore temporal sequences and potential causal pathways.

The observed associations in this study are consistent with existing literature and suggest plausible biological and psychosocial mechanisms. Ageing is a well-established core risk factor for cognitive decline, closely associated with reduced brain reserve and neural ageing.[14] The association between hearing impairment and MCI aligns with longitudinal research by Yu RC et al[15] and others.[16] potentially mediated by increased cognitive load, reduced social engagement, and shared neuropathological processes.[17,18] The link between emotional disorders (eg, anxiety, depression) and MCI has also been frequently reported.[19–21] In the context of multimorbidity, the burden of managing multiple chronic conditions may exacerbate emotional distress, which in turn could negatively impact cognitive function through mechanisms involving stress physiology, inflammation, or changes in brain regions like the hippocampus and prefrontal cortex.

The protective associations observed for higher education, physical exercise, and social activity align with the concept of cognitive reserve – the brain's ability to cope with pathology through pre-existing neural networks and alternative strategies. Higher education, as a proxy for cognitive reserve, may delay the clinical expression of MCI even in the presence of underlying brain changes.[22,23] Social participation is not merely a lifestyle indicator; it actively engages multiple cognitive domains (memory, language, executive function) and may reduce MCI risk via increased neural plasticity, enhanced cognitive stimulation, and reduced loneliness. Our finding that more frequent social activities were protective supports this view. Emotional burden represents a potentially modifiable risk factor. The strong association between emotional disorders and MCI highlights the role of prolonged psychological distress, which may contribute to cognitive decline through hypothalamic-pituitary-adrenal axis dysregulation, chronic inflammation, and reduced neurogenesis.[24] From a healthy ageing perspective, our findings underscore that cognitive health in multimorbid older adults is not determined solely by physical diseases but also by sensory function, mental health, and social-behavioural factors. A holistic approach, integrating psychological support, social engagement, and lifestyle promotion, is essential for dementia prevention and aligns with the World Health Organization's framework for healthy ageing.[25]

Based on the above factors, this study developed and preliminarily validated a visual nomogram to estimate the probability of MCI in older adults with multimorbidity. The strength of the nomogram lies in its ability to integrate multiple factors into a single, accessible visual tool that could, after rigorous prospective validation, potentially aid in risk stratification in clinical settings.[26–28] Internal validation using bootstrapping suggested minimal overfitting, and external validation in an independent cohort from a different department within the same hospital showed promising discriminative ability (AUC=0.832) and calibration.

However, several important limitations must be acknowledged. First, the cross-sectional design fundamentally limits causal inference and leaves open the possibility of reverse causality and unmeasured confounding. Second, the sample was recruited from a single center, which may affect the generalizability of the findings. Third, the external validation cohort, while independent, was relatively small (n=68), leading to less precise performance estimates (wide confidence intervals) and limiting the robustness of the calibration assessment. Fourth, the assessment of some key variables, such as physical activity, social engagement, and emotional disorders, relied on a non-validated questionnaire developed through expert consultation. The use of comprehensive, validated scales in future work would enhance the precision of these measurements. Furthermore, while our model identified several key predictors, it is by no means exhaustive. Other potentially influential variables, such as specific combinations of chronic conditions (eg, the confluence of cardiovascular and metabolic diseases), genetic predispositions (eg, ApoE ε4 status), detailed nutritional status, and systemic inflammatory biomarkers, were not included in our analysis. Their exclusion was primarily due to our focus on creating a parsimonious model with easily obtainable clinical data and constraints related to the sample size. Future studies with larger, more comprehensively phenotyped cohorts are warranted to explore the incremental predictive value of these sophisticated factors and to further refine the model. Fifth, as noted in the discussion, we were unable to perform a direct head-to-head comparison between our nomogram and established general cognitive risk scores due to the absence of key variables required for calculating those scores (eg, specific genetic data, detailed blood lipid profiles) in our dataset.

While the primary aim of our study was to develop a novel, specific tool rather than to validate existing ones, this comparison remains an important future step to definitively quantify the incremental value of our model in clinical practice. Finally, the clinical utility and usability of the nomogram have not been tested in real-world practice; its impact on clinician behavior and patient outcomes remains unknown.

The factors identified in this study, while associative, highlight potential targets for mitigating cognitive risk in older adults with multimorbidity. To translate these findings into clinical practice, future research should prioritize several key areas. First, longitudinal studies are essential to confirm the temporal relationship and potential causal role of these factors, particularly for modifiable ones such as hearing impairment, emotional disorders, and levels of physical and social activity. Subsequently, the clinical utility of the nomogram must be prospectively evaluated to determine if its use in real-world settings, such as geriatric or primary care clinics, actually improves the efficiency of identifying high-risk individuals and leads to better patient outcomes. Finally, the most critical step will be the design and implementation of interventional studies. These trials are needed to test whether addressing these specific factors—for instance, through systematic hearing rehabilitation, management of emotional disorders, or promotion of physical and social engagement—can effectively prevent or delay the onset of MCI in this vulnerable population. Our findings thus provide a rationale and a structured tool for focusing these future investigations.

Conclusion

This cross-sectional study identified several factors associated with MCI in older adults with multimorbidity and developed a preliminary nomogram model that demonstrated good predictive performance in our sample. The model serves as a visual tool that facilitates multi-factor risk assessment. However, the cross-sectional design precludes causal inference, and the model requires further validation. This study lays the groundwork for future research aimed at verifying these associations longitudinally, testing the model's utility in prospective settings, and ultimately determining whether addressing these factors can improve cognitive outcomes in this vulnerable population.

Data Sharing Statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Affiliated Kangning Hospital of Wenzhou Medical University (No. KN-2022-012). All participants provided written informed consent, and the study was performed following the principles of the Declaration of Helsinki. All data collected from subjects remained anonymous and confidential to protect their privacy.

Disclosure

The authors declare that they have no competing interests.

References

1. Zhang LX, Hou SB, Zhao FF, et al. Development and validation of a hyperlipidemia risk prediction model for middle-aged and older adult Chinese using 2015 CHARLS data. *Front Public Health*. 2025;13:1420596. doi:10.3389/fpubh.2025.1420596
2. Rosset F, Mastorino L, Dapavo P, et al. Impact of comorbidities in elderly and frail patients and response to biological therapy in psoriasis. *Exp Dermatol*. 2023;32(7):1162–1164. doi:10.1111/exd.14822
3. Jongsiriyanyong S, Limpawattana P. Mild cognitive impairment in clinical practice: a review article. *Am J Alzheimers Dis Other Demen*. 2018;33(8):500–507. doi:10.1177/1533317518791401
4. Amini N, Ibn Hach M, Lapauw L, et al. Meta-analysis on the interrelationship between sarcopenia and mild cognitive impairment, Alzheimer's disease and other forms of dementia. *J Cachexia Sarcopenia Muscle*. 2024;15(4):1240–1253. doi:10.1002/jcsm.13485
5. Raimo S, Maggi G, Ilardi CR, et al. The relation between cognitive functioning and activities of daily living in normal aging, mild cognitive impairment, and dementia: a meta-analysis. *Neurol Sci*. 2024;45(6):2427–2443. doi:10.1007/s10072-024-07366-2
6. Azizan Z, Bazrgar M, Bazgir N, et al. Osteopontin in Alzheimer's disease: a double-edged sword in neurodegeneration and neuroprotection-a systematic review. *CNS Neurosci Ther*. 2025;31(2):e70269. doi:10.1111/cns.70269

7. Hainsworth AH, Markus HS, Schneider JA. Cerebral small vessel disease, hypertension, and vascular contributions to cognitive impairment and dementia. *Hypertension*. 2024;81(1):75–86. doi:10.1161/HYPERTENSIONAHA.123.19943
8. Riley RD, Ensor J, Snell KI, et al. Calculating the sample size required for developing a clinical prediction model. *BMJ*. 2020;368:m44.
9. Katabathula S, Davis PB, Xu R. Comorbidity-driven multi-modal subtype analysis in mild cognitive impairment of Alzheimer's disease. *Alzheimers Dement*. 2023;19(4):1428–1439. doi:10.1002/alz.12792
10. Nguyen TT, Hoang CBD, Hoang Le MD, et al. Assessing cognitive decline in Vietnamese older adults using the Montreal Cognitive Assessment-Basic (MoCA-B) and Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) during the COVID-19 pandemic: a feasibility study. *Clin Neuropsychol*. 2023;37(5):1043–1061. doi:10.1080/13854046.2023.2192418
11. Dementia and Cognitive Impairment Group, Neurology Branch, Chinese Medical Association. Chinese expert consensus on the diagnosis and treatment of Alzheimer's disease–related mild cognitive impairment, 2021. *Chin J Neurol*. 2022;55(5):421–440.
12. Qiu X, Liang J, Luo L, et al. Patterns of social participation among older adults with chronic multimorbidity in the community: a qualitative study. *Int J Nurs Stud*. 2026;174:105279. doi:10.1016/j.ijnurstu.2025.105279
13. Wang T, He H, Shi Y, et al. Prevalence, incidence and modifiable factors for subtypes of mild cognitive impairment: results from the longitudinal ageing study in China. *Gen Psychiatr*. 2025;38(2):e101736. doi:10.1136/gpsych-2024-101736
14. Islam N, Hashem R, Gad M, et al. Accuracy of the montreal cognitive assessment tool for detecting mild cognitive impairment: a systematic review and meta-analysis. *Alzheimers Dement*. 2023;19(7):3235–3243. doi:10.1002/alz.13040
15. Yu RC, Proctor D, Soni J, et al. Adult-onset hearing loss and incident cognitive impairment and dementia - A systematic review and meta-analysis of cohort studies. *Ageing Res Rev*. 2024;9(12):1023–1028.
16. Asakawa T, Yang Y, Xiao Z, et al. Stumbling blocks in the investigation of the relationship between age-related hearing loss and cognitive impairment. *Perspect Psychol Sci*. 2024;19(1):137–150. doi:10.1177/17456916231178554
17. Grenier B, Berr C, Goldberg M, et al. GDF1 ameliorates cognitive impairment induced by hearing loss. *Nat Aging*. 2024;4(4):568–583. doi:10.1038/s43587-024-00592-5
18. Wu F, Zhou C. Hearing impairment and cognitive function: mediating role of social isolation and depression. *Am J Alzheimers Dis Other Demen*. 2024;39:15333175241227318. doi:10.1177/15333175241227318
19. Nguyen L, Walters J, Hutchinson E, et al. Executive functioning in individuals with generalized anxiety disorder: a systematic review and meta-analysis. *J Affect Disord*. 2025;389:119683. doi:10.1016/j.jad.2025.119683
20. Rhee TG, Shim SR, Manning KJ, et al. Neuropsychological assessments of cognitive impairment in major depressive disorder: a systematic review and meta-analysis with meta-regression. *Psychother Psychosom*. 2024;93(1):8–23. doi:10.1159/000535665
21. Rajji TK, Bowie CR, Herrmann N, et al. Slowing cognitive decline in major depressive disorder and mild cognitive impairment: a randomized clinical trial. *JAMA Psychiatry*. 2025;82(1):12–21. doi:10.1001/jamapsychiatry.2024.3241
22. Bozanic A, Toro P, Bello-Lepe S, et al. Cognitive impairment with type 2 diabetes mellitus among community-dwelling older adults in chile: prevalence, risk factors and cognitive characteristics. *Front Hum Neurosci*. 2023;16:1070611. doi:10.3389/fnhum.2022.1070611
23. Song M, Wang YM, Wang R, et al. Prevalence and risks of mild cognitive impairment of Chinese community-dwelling women aged above 60 years: a cross-sectional study. *Arch Womens Ment Health*. 2021;24(6):903–911. doi:10.1007/s00737-021-01137-0
24. Boa Sorte Silva NC, Barha CK, Erickson KI, et al. Physical exercise, cognition, and brain health in aging. *Trends Neurosci*. 2024;47(6):402–417. doi:10.1016/j.tins.2024.04.004
25. Vítor J, Melita C, Rodrigues M, et al. Physical activity in vascular cognitive impairment: systematic review with meta-analysis. *J Stroke Cerebrovasc Dis*. 2023;32(8):1071–1076. doi:10.1016/j.jstrokecerebrovasdis.2023.107133
26. Cai ZM, Lin HX, Li ZX, et al. A prediction nomogram for postoperative gastroparesis syndrome in right colon cancer: a retrospective study. *Langenbecks Arch Surg*. 2023;13(1):148–153. doi:10.1007/s00423-023-02885-6
27. Xie W, Li Y, Meng X, et al. Machine learning prediction models and nomogram to predict the risk of in-hospital death for severe DKA: a clinical study based on MIMIC-IV, eICU databases, and a college hospital ICU. *Int J Med Inform*. 2023;9(17):1050–1055.
28. Panelli DM, Sherwin EB, Lee CJ, et al. Clinical factors associated with a positive postpartum depression screen in people with cardiac disease during pregnancy. *Curr Res Psychiatry*. 2022;2(2):25–29. doi:10.46439/Psychiatry.2.027