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## Research Report

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# Cognitive Reserve Relationship with Physical Performance in Dementia-Free Older Adults: The MIND-China Study

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### Abstract.

**Background:** Cognitive reserve (CR) may be beneficial to the physical function of the elderly.

**Objective:** We aimed to examine the association of CR proxies and composite CR capacity with physical function in older adults while considering age and sex.

**Methods:** This population-based cross-sectional study included 4,714 participants living in rural China (age  $\geq 60$  years) who were dementia-free. Structural equation modeling was used to generate a composite CR score by integrating early-life education, midlife occupational complexity, and late-life mental activity and social support. The Short Physical Performance Battery (SPPB) measured physical function. Data were analyzed using linear regression models.

**Results:** Greater educational attainment and mental activity were associated with higher composite SPPB scores and those of its three subtests ( $p < 0.05$ ). Skilled occupations were associated with higher SPPB, chair stand, and walking speed scores, while greater social support was associated with higher scores for SPPB and chair stand ( $p < 0.05$ ). Each 1-point increase in composite CR score (range:  $-0.77$  to  $1.03$ ) was linearly associated with a multivariable-adjusted  $\beta$ -coefficient of  $0.74$  (95% confidence interval (CI):  $0.58$ – $0.89$ ) for total SPPB score,  $0.16$  ( $0.10$ – $0.22$ ) for balance test,  $0.40$  ( $0.32$ – $0.48$ ) for chair stand,

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and 0.17 (0.12–0.23) for walking speed. The association between higher composite CR and total SPPB scores was more prominent in those  $\geq 75$  years than those aged 60–74 years ( $p < 0.01$ ). There was no statistical interaction of composite CR score and sex in physical function.

**Conclusions:** High CR is associated with better physical function, especially among older adults ( $\geq 75$  years).

**Keywords:** Alzheimer's disease, cognitive reserve, physical fitness, population-based study

## INTRODUCTION

In aging populations, a decline in physical function occurs, manifesting as slow gait speed, poor endurance, and muscle weakness that can amplify the risk for adverse clinical outcomes such as falls, fractures, institutionalization, and mortality.<sup>1</sup> The Short Physical Performance Battery (SPPB), which is easily applied, has been recommended as a functional test to assess balance, strength, and gait.<sup>2</sup> A population-based cohort study has suggested that lower SPPB scores are associated with higher mortality and an increased risk of frailty and disability in older adults.<sup>2</sup> Identifying modifiable factors related to physical function in older adults is of great importance.

Cognitive reserve (CR) capacity refers to the adaptability of cognitive processes that helps to explain differential susceptibility of cognitive function to physiological or pathological brain aging.<sup>3</sup> Several intellectually stimulating factors, such as education, occupational complexity, and rich social networks, have been considered proxies of CR capacity.<sup>4,5</sup> Given that high CR capacity is associated with better late-life cognitive function<sup>6</sup> and that cognitive and physical dysfunction are closely related,<sup>7</sup> it is plausible to expect that lifelong CR may help preserve physical function into late life. However, few population-based studies have explored the influence of the accumulation of CR throughout life on physical function in later life. Both CR proxies and physical function are strongly related to age and sex. The effect of CR indicators such as education on the conversion from mild cognitive impairment to normal cognition is mainly seen in those younger than 90 years old; additionally, the associations of CR with physical and cognitive activity reserve are more pronounced in females than males.<sup>8–10</sup> Because of this, it is worthwhile to explore whether the relationship between composite CR capacity and physical function may vary with age and sex.

The current population-based study was designed to examine the association of individual CR proxies and composite CR capacity with physical perfor-

mance among community-residing older adults, and whether they are influenced by age or sex. We hypothesized that higher levels of CR proxies and composite CR capacity would be associated with preserved physical function and that such associations might vary by age and sex.

## METHODS

### *Study design and participants*

This population-based cross-sectional study used data from multimodal interventions to identify factors that delay dementia and disability in rural China (MIND-China),<sup>11</sup> an ongoing project in the World-Wide FINGERS Network.<sup>12</sup> In brief, from March to September 2018, a total of 5,765 participants aged 60 years or older living in the 52 villages of Yanlou Town (western Shandong, China) undertook multidisciplinary assessments. Of these, 1,051 persons were excluded because of prevalent dementia ( $n = 307$ ), severe mental diseases ( $n = 49$ ), or missing information on CR proxies ( $n = 494$ ) and SPPB tests ( $n = 201$ ), leaving a total of 4,714 participants in the current analysis (Fig. 1).

### *Data collection and assessment*

From March to September 2018, trained medical staff collected data through face-to-face interviews, clinical examinations, neuropsychological testing, and laboratory tests in collaboration with laboratory technicians at the local town hospital, as reported previously.<sup>13</sup> Sociodemographic, clinical, and neuropsychological data were collected using a structured questionnaire. We collected data on sociodemographic characteristics (e.g., age and sex), lifestyle factors (e.g., smoking, alcohol drinking, and body mass index), and health conditions (e.g., hypertension, diabetes mellitus, hyperlipidemia, and cardiovascular disorders).

The Ethics Committee at Shandong Provincial Hospital affiliated with Shandong University approved the MIND-China protocol. Written

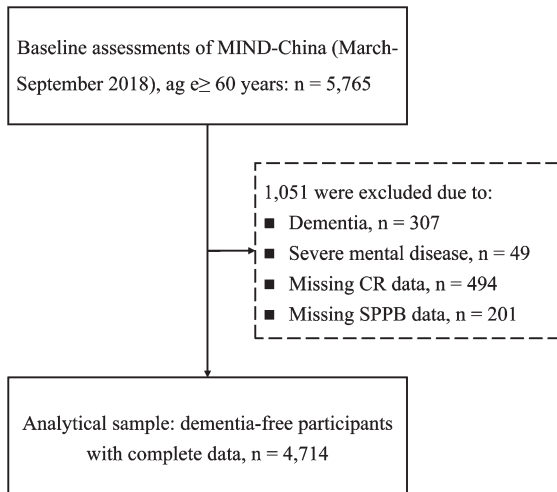


Fig. 1. Flowchart of study participants. MIND-China, Multimodal Interventions to delay dementia and disability in Rural China; CR, cognitive reserve; SPPB, Short Physical Performance Battery.

informed consent was obtained from all participants. MIND-China was registered in the Chinese Clinical Trial Registry (registration no.: ChiCTR1800017758).

#### Assessment of CR proxies

Education was measured as the maximum years of formal schooling<sup>14</sup> categorized into no formal schooling, primary school (1–5 years), and middle school or above ( $\geq 6$  years). Occupational complexity was determined by asking participants about the type of their longest-held occupation, which was then defined as either skilled or unskilled.

Late-life mental activity was assessed by asking participants whether they engaged in the nine activities, including playing mahjong, playing cards, playing chess, listening to operas, watching TV, reading newspapers, playing tai chi, bird walking, and joining religious gatherings. Of these, walking birds and practicing tai chi were excluded from analysis due to their rarity. Finally, the variable of mental activity was dichotomized into high (those participated in any of the seven activities  $\geq 1$  day/week) or low (those  $< 1$  day/week) according to the frequency of activities.<sup>11</sup> Late-life social support was assessed using the Social Support Rating Scale (SSRS)<sup>15</sup> which has been validated in the Chinese population.<sup>16</sup> The total SSRS score ranged from 12 to 60, with a higher score indicating more social support. Social support was dichotomized into low and high according to the mean SSRS score (47.17).

Previous literature has indicated that early-life education, midlife occupational complexity, and late-life mental activity and social support can be considered CR proxies that can be incorporated into a structural equation model to generate composite CR.<sup>17</sup> In the present study, all the four CR proxies were treated as categorical variables in a structural equation model and full information maximum likelihood estimation was used to generate a best-fit model. Multiple indices were used to evaluate model fit: chi-square ( $\chi^2$ ) goodness of fit, the comparative fit index ( $> 0.95$ ), the Tucker-Lewis Index  $> 0.95$ , and the root-mean-squared error of approximation  $< 0.06$ .<sup>18</sup> We assessed the associations between CR proxies and the underlying latent variable as the composite CR score. The model demonstrated a robust fit:  $\chi^2$  goodness of fit = 1.955, root-mean-squared error of approximation = 0.014, comparative fit index = 0.999, and Tucker-Lewis index = 0.994. The correlation coefficients of 0.86 for education, 0.41 for occupational complexity, and 0.19 for mental activity and social support indicated their respective weights to the composite CR score.  $e_1$ ,  $e_2$ ,  $e_3$ , and  $e_4$  were the residual variances of the measured variables (Fig. 2). Finally, we summed the products of the four proxies and their respective weights to calculate the composite CR scores as continuous variables and generated categorical variables using tertiles (reference: lowest tertile). The composite CR value of each participant was unique, ranging from  $-0.77$  to  $1.03$  (mean value =  $0.00$ , standard deviation =  $0.54$ ). Higher scores indicated greater CR capacity.

#### Assessment of physical function

We used the SPPB test to measure physical function, which consisted of three subtests: a standing balance test, sitting-to-standing five times (chair stand), and a 4 m walking test.<sup>19</sup> The scores of each subtest ranged from 0 to 4 and were summed to provide a total SPPB score (range: 0–12), with a higher score indicating better physical performance.

#### Assessment of vascular risk factors and multimorbidity

Body mass index was calculated as weight (kg) divided by height squared ( $m^2$ ). We categorized smoking and alcohol drinking as either ever or never. A total of 23 chronic health conditions were defined based on clinical examination, instrumental examination (e.g., electrocardiogram and abdomi-

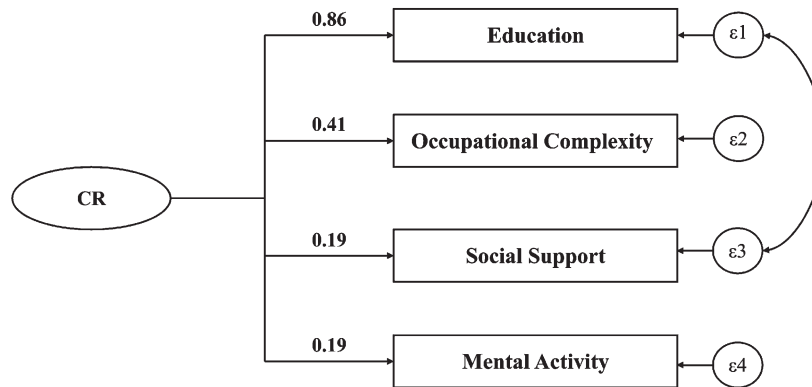


Fig. 2. Standardized estimates from the structural equation model with 4 observable cognitive reserve factors of a latent reserve construct. The values indicate the loadings of the 4 factors to cognitive reserve.  $\epsilon_1$ ,  $\epsilon_2$ ,  $\epsilon_3$ , and  $\epsilon_4$  are the residual variances of the measured indicator variables. Structural equation modeling fit statistics:  $\chi^2$  goodness of fit = 1.955, root-mean-squared error of approximation = 0.014, comparative fit index = 0.999, Tucker-Lewis index = 0.994.

nal ultrasound), self-reported health history, use of medications, and laboratory tests. Consistent with previous studies,<sup>20,21</sup> dichotomous ratings (presence or absence) of hypertension, diabetes, hyperlipidemia, ischemic heart disease, atrial fibrillation, stroke, epilepsy, asthma, chronic kidney, thyroid disease, peptic ulcer, degenerative disc disease, gall bladder disease (cholecystitis and cholelithiasis), chronic obstructive pulmonary disease, Parkinson's disease, heart failure, cancer, arthritis, tuberculosis, hepatitis, cataract, glaucoma, and lower extremity varicose veins were used to determine multimorbidity. Multimorbidity was defined as the concurrent presence of two or more of the 23 chronic health conditions in the same individual.<sup>21</sup>

### Statistical analysis

Study participant characteristics were compared across CR levels using one-way analysis of variance and Bartlett's test for continuous variables and Chi-square tests for categorical variables. We employed a general linear model to examine the associations between early-life education, midlife occupational complexity, late-life social support and mental activity, and composite CR capacity (composite CR score and categorical CR levels) with physical function (total SPPB, balance test, chair stand, and walking speed test score). We investigated the interactions of composite CR score with age (60–74 versus  $\geq 75$  years) and sex on physical function. Stratified analyses were performed when statistically significant interactions were detected ( $p < 0.01$ ). We did not examine the interactions between the four individual

CR proxies with age or sex on physical function, taking into account the risk of multiple comparison. The main results from two models were reported: Model 1 was adjusted for age (years) and sex, while Model 2 was additionally adjusted for body mass index, smoking ever, ever drinking alcohol, and multimorbidity, which were reported to be directly associated with physical performance.<sup>22–24</sup> Stata Statistical Software: Release 16.0 (Stata Corp LLC., College Station, TX, USA) was used for all data analyses.

## RESULTS

### Characteristics of study participants

The mean age of the 4,714 participants was 70.22 (standard deviation = 5.33) years; 56.30% were female, and 37.37% had no formal schooling. Compared with participants with low CR, those with a high CR capacity were younger, more likely to be male and educated, more likely to smoke, drink alcohol, engage in complicated work and mental activities, and had a higher SSRS score and a higher body mass index ( $p < 0.05$ ) (Table 1). The prevalence of multimorbidity did not differ significantly between the different levels of CR capacity ( $p > 0.05$ ).

### Associations of CR with physical function

Among the four CR proxies, education and mental activity exhibited significant correlations with higher physical function in terms of total SPPB, balance test, chair stand, and walking speed test scores. Additionally, having a skilled occupation (versus un-skilled)

Table 1  
Characteristics of study participants in the total sample and by levels of cognitive reserve

Characteristics	Total sample, <i>n</i> = 4,714	Levels of cognitive reserve, tertiles			<i>P</i>
		Lower, <i>n</i> = 1,673	Medium, <i>n</i> = 1,815	Upper, <i>n</i> = 1,226	
Age (y), mean (SD)	70.22 (5.33)	70.55 (6.00)	70.40 (4.63)	69.48 (5.26)	<0.001
Female, <i>n</i> (%)	2,654 (56.30)	1,486 (88.82)	962 (53.00)	206 (16.80)	<0.001
Ever smoking, <i>n</i> (%) <sup>a</sup>	1,752 (37.17)	188 (11.24)	716 (39.45)	848 (69.17)	<0.001
Ever alcohol drinking, <i>n</i> (%) <sup>a</sup>	1,898 (40.26)	253 (15.12)	761 (41.93)	884 (72.10)	<0.001
BMI, Mean (SD) <sup>a</sup>	24.93 (3.74)	25.14 (3.83)	24.77 (3.74)	24.89 (3.62)	0.014
Multimorbidity, (%) <sup>a</sup>	2,753 (58.40)	991 (59.23)	1,068 (58.84)	694 (56.61)	0.251
Education, <i>n</i> (%)					
Illiterate	1,763 (37.40)	1,673 (100.00)	90 (4.96)	0 (0.00)	<0.001
Primary school	2,061 (43.72)	0 (0.00)	1,725 (95.04)	336 (27.41)	<0.001
Middle school and above	890 (18.88)	0 (0.00)	0 (0.00)	890 (72.59)	<0.001
Occupational complexity, <i>n</i> (%)					
Un-Skilled	3,872 (82.14)	1,669 (99.76)	1,716 (94.55)	487 (39.72)	<0.001
Skilled	842 (17.86)	4 (0.24)	99 (5.45)	739 (60.28)	<0.001
Mental activity, <i>n</i> (%)					
Low	427 (9.06)	253 (15.12)	140 (7.71)	34 (2.77)	<0.001
High	4,287 (90.94)	1,420 (84.88)	1,675 (92.29)	1,192 (97.23)	<0.001
Social support, mean (SD)					
Low	1,951 (41.39)	759 (45.37)	787 (43.36)	405 (33.03)	<0.001
High	2,763 (58.61)	914 (54.63)	1,028 (56.64)	821 (66.97)	<0.001
SPPB summary score, mean (SD)	9.51 (2.63)	8.92 (2.72)	9.50 (2.63)	10.35 (2.26)	<0.001
SPPB balance score, mean (SD)	3.46 (1.01)	3.28 (1.10)	3.49 (1.01)	3.66 (0.84)	<0.001
SPPB chair stand score, mean (SD)	2.64 (1.33)	2.36 (1.34)	2.61 (1.33)	3.05 (1.19)	<0.001
SPPB walking speed score, mean (SD)	3.42 (0.88)	3.28 (0.92)	3.40 (0.88)	3.64 (0.76)	0.001

Data were *n* (%), unless otherwise specified. SD, standard deviation; BMI, body mass index; SPPB, Short Physical Performance Battery.

<sup>a</sup>Number of participants with missing values was 11 for alcohol drinking, 1 for smoking, 27 for BMI, and 57 for multimorbidity. In subsequent analyses, the missing values were replaced with a dummy variable.

was significantly correlated with higher total SPPB, chair stand, and walking speed test scores, but not with balance test scores. Higher social support was associated with higher total SPPB and chair stand scores, but not with balance test or walking speed test scores. These associations remained significant after further adjusting for body mass index, smoking, alcohol drinking, and multimorbidity ( $p < 0.05$ , Table 2). A greater composite CR score was correlated with higher total SPPB, balance test, chair stand test, and walking speed test scores, even when controlling for vascular risk factors and multimorbidity (Table 2). Compared with low CR, medium and high CR were both significantly linearly associated with higher total SPPB, balance, chair stand, and walking speed test scores (Table 2).

#### Effects of interaction of CR with age and sex on physical function

There were significant interactions between composite CR score and age in terms of the total SPPB, balance, and walking speed test scores ( $p < 0.01$ ), but not on the chair stand score. Stratifying analysis by age groups suggested that the multivariable-adjusted

$\beta$ -coefficients of total SPPB score that were associated with greater composite CR score were 0.68 (95% CI: 0.51–0.84) in participants aged 60–74 years and 1.26 (95% CI: 0.86–1.67) in those  $\geq 75$  (Fig. 3a). A higher balance test score was associated with a greater composite CR score, with  $\beta$ -coefficients of 0.14 (95% CI: 0.08–0.20) for those aged between 60–74 years and 0.32 (95% CI: 0.15–0.49) for those aged  $\geq 75$  (Fig. 3b). Similarly, a higher walking test score was linked with a greater composite CR score, with  $\beta$ -coefficients of 0.16 (95% CI: 0.10–0.21) for individuals between 60–74 years old and 0.35 (95% CI: 0.21–0.49) for those aged  $\geq 75$  (Fig. 3c). There was no statistical interaction of composite CR score with sex on the total SPPB, balance test, chair stand, or walking speed test scores ( $p > 0.05$ ).

## DISCUSSION

In this large-scale population-based cross-sectional study, we examined the association between CR capacity and physical function among older adults in China as well as the moderating role of age and sex on these relationships. This study highlighted the potential association of greater

Table 2  
Associations of cognitive reserve with physical function (n = 4,714)

Cognitive reserve proxies	No.	β-coefficient (95% confidence interval)							
		SPPB summary score		SPPB balance score		SPPB chair stand score		SPPB walking speed score	
		Model 1	Model 2	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
Education									
Illiterate	1,763	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)
Primary school	2,061	0.34 (0.17, 0.51) <sup>‡</sup>	0.37 (0.20,0.54) <sup>‡</sup>	0.12 (0.05,0.19) <sup>†</sup>	0.13 (0.06,0.19) <sup>‡</sup>	0.16 (0.07,0.25) <sup>‡</sup>	0.18 (0.09,0.26) <sup>†</sup>	0.06 (0.00,0.12)*	0.07 (0.01,0.13)*
Middle school or above	890	0.72 (0.48, 0.96) <sup>‡</sup>	0.78 (0.55,1.02) <sup>‡</sup>	0.16 (0.07,0.26) <sup>†</sup>	0.18 (0.09,0.27) <sup>‡</sup>	0.39 (0.27,0.52) <sup>‡</sup>	0.42 (0.30,0.54) <sup>‡</sup>	0.16 (0.08,0.24) <sup>‡</sup>	0.18 (0.10,0.26) <sup>‡</sup>
Occupational complexity									
Un-skilled	3,872	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)
Skilled	842	0.39 (0.18, 0.59) <sup>‡</sup>	0.41 (0.21,0.61) <sup>‡</sup>	0.03 (−0.05,0.11)	0.03 (−0.05,0.11)	0.23 (0.12,0.33) <sup>‡</sup>	0.24 (0.14,0.34) <sup>‡</sup>	0.13 (0.06,0.20) <sup>‡</sup>	0.14 (0.07,0.21) <sup>‡</sup>
Mental activity									
Low	427	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)
High	4,287	0.47 (0.22,0.72) <sup>‡</sup>	0.52 (0.27,0.76) <sup>‡</sup>	0.17 (0.07,0.27) <sup>†</sup>	0.18 (0.08,0.28) <sup>†</sup>	0.18 (0.05,0.31) <sup>†</sup>	0.20 (0.07,0.33) <sup>†</sup>	0.13 (0.04,0.21) <sup>†</sup>	0.14 (0.06,0.22) <sup>†</sup>
Social support, mean (SD)									
Low	1,951	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)
High	2,763	0.30 (0.15, 0.45) <sup>‡</sup>	0.29 (0.14,0.43) <sup>‡</sup>	0.04 (−0.02,0.10)	0.04 (−0.02,0.10)	0.22 (0.14,0.29) <sup>‡</sup>	0.21 (0.13,0.28) <sup>‡</sup>	0.04 (−0.01,0.09)	0.04 (−0.01,0.09)
Composite CR score									
CR levels, tertiles									
Lower	1,674	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)
Medium	1,815	0.38 (0.21,0.56) <sup>‡</sup>	0.40 (0.23,0.58) <sup>‡</sup>	0.14 (0.07,0.21) <sup>†</sup>	0.14 (0.07,0.21) <sup>†</sup>	0.17 (0.08,0.26) <sup>‡</sup>	0.19 (0.10,0.27) <sup>‡</sup>	0.07 (0.01,0.13)*	0.08 (0.02,0.14) <sup>†</sup>
Upper	1,226	0.93 (0.70,1.15) <sup>‡</sup>	0.98 (0.77,1.20) <sup>‡</sup>	0.20 (0.11,0.29) <sup>‡</sup>	0.21 (0.13,0.30) <sup>‡</sup>	0.50 (0.39,0.61) <sup>‡</sup>	0.53 (0.41,0.64) <sup>‡</sup>	0.23 (0.15,0.30) <sup>‡</sup>	0.24 (0.17,0.32) <sup>‡</sup>
p-for-trend	4,714	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

SPPB, Short Physical Performance Battery; SD, standard deviation; CR, cognitive reserve. \* $p < 0.05$ , <sup>†</sup> $p < 0.01$ , <sup>‡</sup> $p < 0.001$ ; Model 1 was adjusted for age, and sex; Model 2 was additionally adjusted for body mass index, smoking, alcohol drinking, and multimorbidity.

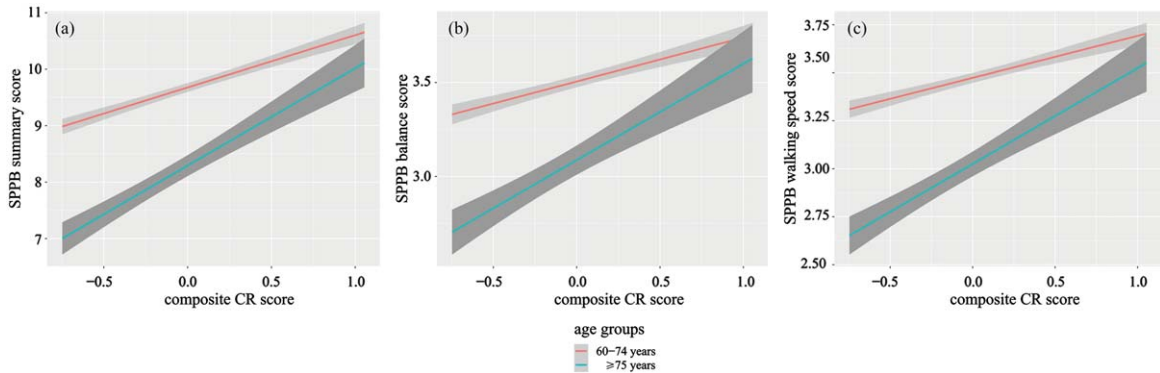


Fig. 3. Associations between composite CR score and SPPB test scores by different age groups. The graphs illustrate the interaction between composite CR score and age on SPPB test performance. The x-axis represents composite CR score, and the y-axis indicates the SPPB summary score (a), SPPB balance score (b), and SPPB walking speed score (c).

lifelong CR capacity with better late-life physical function; this association was stronger in older adults aged 75–84 years than in those aged 60–74. Additionally, individual CR proxies (education, occupational complexity, mental activities, and social support) were associated with better physical function.

Identifying modifiable factors associated with poor physical function is crucial to the health of the older population. A population-based study of older adults in Shanghai found that higher education was associated with greater SPPB scores.<sup>25</sup> In addition, educational attainment is related to better walking speed, greater grip strength, and lower extremity function over time.<sup>26,27</sup> Our results complement these previous studies by showing that education levels of middle school and above was significantly associated with higher total SPPB, balance, chair stand, and walking speed test scores, even in a population with relatively limited education. Our findings were also consistent with several community-based cohort studies showing that social relationships and lifetime occupation were both significantly associated with physical performance.<sup>28,29</sup> In our study, mental activity was significantly correlated with physical function. However, the Chinese Longitudinal Healthy Longevity Survey (CLHLS) did not find a significant association between mental activity and physical performance.<sup>30</sup> There may be several reasons for the different findings across studies. We included people aged 60 years and older in this study, while the CLHLS study only included people aged 65 years and above. In addition, the CLHLS study evaluated physical performance by assessing the Activities of Daily Living and the strength of the upper and

lower limbs and waist, but not balance ability or walking speed, which may have partly contributed to the different results.

We found a close association between higher CR capacity and preserved physical function. Several mechanisms could potentially explain such an association. Individuals with a high level of CR proxies often possess a better socioeconomic status and healthier lifestyles,<sup>31</sup> both of which are closely associated with improved physical function.<sup>32</sup> Second, engaging in mental and social activities can enhance neural networks and boost musculoskeletal functions; these factors are essential for preserving functional independence in late life.<sup>33</sup> Additionally, body movements accompanied by mental activities have the potential to alleviate age-related oxidative damage and chronic inflammation; these movements can promote anabolism, contributing to heightened muscle protein synthesis and postponing disability.<sup>34</sup> Participating in mental activity can not only enhance social participation but also reduce depression, exerting a positive influence on physical function.<sup>35,36</sup> A meta-analysis showed that CR had a protective effect in  $\alpha$ -synuclein disease characterized by motor symptoms and cognitive impairment;<sup>37,38</sup> this finding provides theoretical support for the influence of CR capacity on both physical function and cognitive health. Finally, we observed a significant association with an increased coefficient between CR and physical function even after adjusting for covariates (Model 2). This finding highlights a robust correlation between CR and physical function, reinforcing our hypothesis.

A study conducted by the White House in the United States found a correlation between unhealthy



behaviors (current or recent smoking, non-moderate alcohol drinking) and a decrease in walking speed, with this association having a cumulative effect.<sup>24</sup> Additionally, a prospective study indicated that multimorbidity significantly reduces patients' cognitive function, walking speed, and grip strength.<sup>23</sup> Our study further complements previous findings by demonstrating a stronger correlation between composite CR and SPPB scores after adjusting for vascular risk factors and multimorbidity. However, in our study, the proportions of smoking and alcohol drinking were higher among individuals with high CR. We speculate that this may be because in rural areas, smoking and drinking are often associated with more frequent social activities and higher socioeconomic status; at the same time, smoking and drinking are also often related to greater stress from engaging in more complex occupations.

Age is a critical factor influencing both physical function and cognition.<sup>39</sup> With aging, there is a potential decline in muscle strength, balance, and walking speed, which may be attributed to the gradual decrease in muscle mass and function, reduction in bone density, and degeneration of balance and the nervous system.<sup>40,41</sup> A previous longitudinal study conducted in the USA found an association between high CR capacity and higher walking speed, with age exerting a moderating role.<sup>39</sup> Consistent with the above findings, we also found that the association between composite CR capacity and physical function was stronger in people at advanced age compared to those at younger age. This could be partly explained by a few reasons. First, older individuals, compared with the younger counterparts in our study, might exhibit a lower threshold in physical performance. This observed disparity could potentially magnify the statistical impact of CR capacity. Secondly, individuals aged 75 years or older, possessing lower CR capacity and diminished physical performance, were less inclined to survive. Because of this, survival bias must be taken into account when interpreting the age disparity in the association between CR and physical function.

The main strengths of our study include its large sample of community-based rural-dwelling Chinese older adults with relatively limited access to lifetime CR proxies. In addition, physical function was objectively measured using a standardized test with high reliability. However, our study does have limitations. Some CR proxies such as premorbid intelligence quotient and nutrition intake were not available, which might have led to an underestimation of the true asso-

ciation between CR capacity and physical function. Because of the nature of cross-sectional design, any of the observed associations between CR capacity and physical function can also not be interpreted as causal relationships. Future prospective cohort studies are imperative to establish the potential temporal association between CR capacity and physical function.

In conclusion, this population-based study showed that a high lifelong reserve CR capacity was associated with better late-life physical performance and that this association was more pronounced in those  $\geq 75$  years old. Further prospective cohort studies are needed to comprehensively explore the complex interplay between age, CR, and physical function, which will facilitate the development of interventions towards achieving longer and healthier lives.

## AUTHOR CONTRIBUTIONS

Qiwei Dong (Conceptualization; Data curation; Investigation; Methodology; Writing – original draft); Yuanjing Li (Data curation; Methodology); Yiming Song (Investigation); Yu Zhang (Investigation); Xiaodong Han (Investigation); Yifei Ren (Investigation); Jiafeng Wang (Investigation); Xiaojuan Han (Conceptualization; Supervision; Writing – review & editing); Yifeng Du (Conceptualization; Supervision).

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## CONFLICT OF INTEREST

The authors have no conflict of interest to report.

## DATA AVAILABILITY

The data supporting the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

## REFERENCES

- Cooper R, Kuh D and Hardy R. Objectively measured physical capability levels and mortality: systematic review and meta-analysis. *BMJ* 2010; 341: c4467.
- Fortes-Filho SQ, Aliberti MJR, Apolinario D, et al. Role of gait speed, strength, and balance in predicting adverse outcomes of acutely ill older outpatients. *J Nutr Health Aging* 2020; 24: 113–118.
- Stern Y, Arenaza-Urquijo EM, Bartrés-Faz D, et al. Whitepaper: Defining and investigating cognitive reserve, brain reserve, and brain maintenance. *Alzheimers Dement* 2020; 16: 1305–1311.
- Stern Y, Gurland B, Tatemichi TK, et al. Influence of education and occupation on the incidence of Alzheimer's disease. *JAMA* 1994; 271: 1004–1010.
- Wang Y, Chen X and Hu Y. Relationship between social support and 7-year trajectories of cognitive decline: results from the China Health and Retirement Longitudinal Study. *J Epidemiol Community Health* 2023; 77: 578–586.
- Clare L, Wu Y-T, Teale JC, et al. Potentially modifiable lifestyle factors, cognitive reserve, and cognitive function in later life: A cross-sectional study. *PLoS Med* 2017; 14: e1002259.
- Clouston SAP, Brewster P, Kuh D, et al. The dynamic relationship between physical function and cognition in longitudinal aging cohorts. *Epidemiol Rev* 2013; 35: 33–50.
- PaJ, Aslanyan V, Casaletto KB, et al. Effects of sex, APOE4, and lifestyle activities on cognitive reserve in older adults. *Neurology* 2022; 99: e789–e798.
- Holtzer R, Choi J, Motl RW, et al. Individual reserve in aging and neurological disease. *J Neurol* 2023; 270: 3179–3191.
- Iraniparast M, Shi Y, Wu Y, et al. Cognitive reserve and mild cognitive impairment: predictors and rates of reversion to intact cognition vs progression to dementia. *Neurology* 2022; 98: e1114–e1123.
- Wang Y, Han X, Zhang X, et al. Health status and risk profiles for brain aging of rural-dwelling older adults: Data from the interdisciplinary baseline assessments in MIND-China. *Alzheimers Dement (N Y)* 2022; 8: e12254.
- Kivipelto M, Mangialasche F, Snyder HM, et al. World-Wide FINGERS Network: A global approach to risk reduction and prevention of dementia. *Alzheimers Dement* 2020; 16: 1078–1094.
- Cong L, Ren Y, Hou T, et al. Use of cardiovascular drugs for primary and secondary prevention of cardiovascular disease among rural-dwelling older Chinese adults. *Front Pharmacol* 2020; 11: 608136.
- Ren Y, Dong Y, Hou T, et al. Prevalence, incidence, and progression of cognitive impairment, no dementia among rural-dwelling Chinese older adults. *J Alzheimers Dis* 2022; 85: 1583–1592.
- Xiao SY. The theoretical basis and applications of Social Support Rating Scale (in Chinese). *J Clin Psychiatry* 1994; 98–100.
- Li Z, Yi X, Zhong M, et al. Psychological distress, social support, coping style, and perceived stress among medical staff and medical students in the early stages of the COVID-19 epidemic in China. *Front Psychiatry* 2021; 12: 664808.
- Xu H, Yang R, Qi X, et al. Association of lifespan cognitive reserve indicator with dementia risk in the presence of brain pathologies. *JAMA Neurol* 2019; 76: 1184–1191.
- Hu L, Bentler PM. Cutoff criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. *Struct Equ Modeling* 1999; 6: 1–55.
- Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol* 1994; 49: M85–M94.
- Han Q, Han X, Wang X, et al. Association of accelerometer-measured sedentary behavior patterns with nonalcoholic fatty liver disease among older adults: The MIND-China Study. *Am J Gastroenterol* 2023; 118: 569–573.
- Ren Y, Li Y, Tian N, et al. Multimorbidity, cognitive phenotypes, and Alzheimer's disease plasma biomarkers in older adults: A population-based study. *Alzheimers Dement* 2024; 20: 1550–1561.
- Skow LF, Sharrett AR, Gottesman RF, et al. Mid-life vascular risk and rate of physical function decline among older adults: The Atherosclerosis Risk in Communities (ARIC) Study. *J Gerontol A Biol Sci Med Sci* 2024; 79.
- Wei MY, Kabeto MU, Langa KM, et al. Multimorbidity and physical and cognitive function: performance of a new multimorbidity-weighted index. *J Gerontol A Biol Sci Med Sci* 2018; 73: 225–232.
- Sabia S, Elbaz A, Rouveau N, et al. Cumulative associations between midlife health behaviors and physical functioning in early old age: a 17-year prospective cohort study. *J Am Geriatr Soc* 2014; 62: 1860–1868.
- Zhang P, Abudukelimu N, Sali A, et al. Sociodemographic features associated with the MoCA, SPPB, and GDS scores in a community-dwelling elderly population. *BMC Geriatr* 2023; 23: 557.
- Haas SA, Krueger PM and Rohlfen L. Race/ethnic and nativity disparities in later life physical performance: the role of health and socioeconomic status over the life course. *J Gerontol B Psychol Sci Soc Sci* 2012; 67: 238–248.
- Coppin AK, Ferrucci L, Lauretani F, et al. Low socioeconomic status and disability in old age: evidence from the InChianti study for the mediating role of physiological impairments. *J Gerontol A Biol Sci Med Sci* 2006; 61: 86–91.
- Jiao D, Watanabe Miura K, Sawada Y, et al. Changes in social relationships and physical functions in community-dwelling older adults. *J Nurs Res* 2022; 30: e228.
- Russo A, Onder G, Cesari M, et al. Lifetime occupation and physical function: a prospective cohort study on persons aged 80 years and older living in a community. *Occup Environ Med* 2006; 63: 438–442.
- Ren Z, Zhang X, Li Y, et al. Relationships of leisure activities with physical and cognitive functions among Chinese older

- adults: A prospective community-based cohort study. *Aging Ment Health* 2023; 27: 736–744.
31. Turrell G, Lynch JW, Kaplan GA, et al. Socioeconomic position across the lifecourse and cognitive function in late middle age. *J Gerontol B Psychol Sci Soc Sci* 2002; 57: S43–S51.
  32. Zang E, Shi Y, Wang X, et al. Trajectories of physical functioning among US adults with cognitive impairment. *Age Ageing* 2022; 51: afac139.
  33. Falk EB and Bassett DS. Brain and social networks: fundamental building blocks of human experience. *Trends Cogn Sci* 2017; 21: 674–690.
  34. Fancourt D, Aughterson H, Finn S, et al. How leisure activities affect health: a narrative review and multi-level theoretical framework of mechanisms of action. *Lancet Psychiatry* 2021; 8: 329–339.
  35. Tomioka K, Kurumatani N and Hosoi H. Association between social participation and instrumental activities of daily living among community-dwelling older adults. *J Epidemiol* 2016; 26: 553–561.
  36. Tomioka K, Kurumatani N and Hosoi H. Relationship of having hobbies and a purpose in life with mortality, activities of daily living, and instrumental activities of daily living among community-dwelling elderly adults. *J Epidemiol* 2016; 26: 361–370.
  37. Saywell I, Child B, Foreman L, et al. Influence of cognitive reserve on cognitive and motor function in  $\alpha$ -synucleinopathies: A systematic review protocol. *Ann N Y Acad Sci* 2023; 1522: 15–23.
  38. Gu L and Xu H. Effect of cognitive reserve on cognitive function in Parkinson's disease. *Neurol Sci* 2022; 43: 4185–4192.
  39. O'Brien C and Holtzer R. Cognitive reserve moderates associations between walking performance under single- and dual-task conditions and incident mobility impairment in older adults. *J Gerontol A Biol Sci Med Sci* 2021; 76: e314–e320.
  40. Corish CA and Bardon LA. Malnutrition in older adults: screening and determinants. *Proc Nutr Soc* 2019; 78: 372–379.
  41. Medina-Gomez C, Kemp JP, Trajanoska K, et al. Life-course genome-wide association study meta-analysis of total body BMD and assessment of age-specific effects. *Am J Hum Genet* 2018; 102.