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Association of Physical-Mental Comorbidity with Cognitive Decline among Middle-Aged and Older Adults in China, India, and Indonesia: Postprint

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Abstract

Background Domestic and international research evidence demonstrates that multimorbidity is closely associated with brain health in older populations. Currently, few studies have examined the simultaneous impact of physical and mental illnesses on cognitive impairment.

Objective To explore the association between physical-mental multimorbidity and cognitive decline among middle-aged and elderly populations in China, India, and Indonesia.

Methods This study utilized nationally representative survey databases from the China Health and Retirement Longitudinal Study (CHARLS, 2015), the Longitudinal Aging Study in India (LASI, 2017-2018), and the Indonesia Family Life Survey (IFLS, 2014-2015), with a total of 73,119 respondents included. Cognitive function was assessed across three dimensions: temporal orientation, word recall, and calculation ability. Five categories of physical-mental multimorbidity were constructed based on the number of reported chronic non-communicable diseases and the presence of depressive symptoms. Multiple linear regression models were employed to investigate the relationship between physical-mental multimorbidity and cognitive decline.

Results The Chinese sample included 9,951 middle-aged and elderly respondents with an average cognitive function score of (54.7$±19.9); *theIndiansampleincluded*54, 802*respondentswithana*
agedandelderlyrespondentswithphysical−mentalmultimorbidityexhibitedsignificantlylowercognitivefunct
−6.99, 95 = −2.76, 95 $=-2.75, 95%CI=-4.10~-1.41) (P<0.05).

Conclusion Physical-mental multimorbidity is associated with cognitive decline among middle-aged and elderly populations in China, India, and Indonesia, with a more pronounced effect observed in women. Addressing and proactively

managing mental health issues in patients with multimorbidity may reduce the risk of cognitive impairment and dementia in older populations.

Full Text

Association of Mental-Physical Multimorbidity with Cognitive Decline among Middle-Aged and Older Adults in China, India, and Indonesia

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Abstract

Background: Evidence from existing literature demonstrates that multimorbidity is closely linked to brain health among older adults. However, few studies have examined the combined impacts of physical and mental illnesses on cognitive impairment.

Objective: To explore the association between mental-physical multimorbidity and cognitive decline among middle-aged and older adults in China, India, and Indonesia.

Methods: This study utilized nationally representative survey data from the China Health and Retirement Longitudinal Study (CHARLS, 2015), the Longitudinal Aging Study in India (LASI, 2017–2018), and the Indonesian Family Life Survey (IFLS, 2014–2015), comprising a total of 73,119 respondents. Cognitive function was assessed across three domains: time orientation, word recall, and numeracy. Five categories of mental-physical multimorbidity were constructed

based on the number of reported chronic non-communicable diseases and the presence of depressive symptoms. Multivariable linear regression models were applied to examine the relationship between mental-physical multimorbidity and cognitive decline.

Results: The sample included 9,951 middle-aged and older adults from China with a mean cognitive function score of (54.7±19.9); 54, 802*fromIndiawithameanscoreof*(51.1±20.0); *and*8, 4
physicalmultimorbidityhadsignificantlylowercognitivefunctionthanthosewithoutchronicdiseasesinChina(
−6.99, 95 = −2.76, 95 =-2.75, 95%CI=-4.10~-1.41) (all P<0.05).

Conclusion: Mental-physical multimorbidity is associated with cognitive decline among middle-aged and older adults in China, India, and Indonesia, with a more pronounced effect among females. Addressing mental health problems among patients with multimorbidity may reduce the risk of cognitive impairment and dementia in older populations.

Keywords: Multimorbidity; Middle-aged; Aged; Mental-physical multimorbidity; Cognitive performance; China; India; Indonesia

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Introduction

Population aging is accelerating globally. By 2050, adults aged 65 and older are projected to account for 16% of the total population, with even higher proportions expected in East and Southeast Asia, rising from 13% in 2022 to 26% in 2025 [1]. Population aging is associated with various age-related health issues, including chronic diseases, multimorbidity (defined as the coexistence of two or more chronic non-communicable diseases), mental health problems, and cognitive decline [2,3]. Mild cognitive impairment represents an intermediate stage between normal aging and dementia and serves as a critical clinical manifestation and risk factor for dementia. Dementia, characterized by progressive cognitive decline that limits individuals' ability to function independently [4], constitutes a major cause of care dependency and disability, imposing substantial health and caregiving burdens on patients and their families [5]. Therefore, it is essential to monitor the risk of moderate to severe dementia among older populations, particularly during the critical window before comprehensive cognitive decline, by assessing cognitive function levels, exploring key factors influencing cognitive deterioration, and implementing individualized cognitive care training to prevent dementia.

The growing burden of cognitive diseases and brain health issues has garnered increasing attention from scholars and society, with challenges in developing countries demanding particular consideration. Research by Shi et al. [6] indicates that the overall prevalence of mild cognitive impairment among Chinese older adults is 19%, with an increasing trend over the past decade (ranging from 11% to 28%) and substantial variation across provinces and regions. In most cases, cognitive impairment and dementia among older adults can be delayed or

prevented through control of modifiable risk factors, including individual characteristics (such as education level) and behavioral lifestyles (such as smoking, physical inactivity, and social isolation). Previous studies have also identified that cardiometabolic multimorbidity and genetic factors significantly influence dementia risk [3,7]. However, the complex relationships among physical multimorbidity, depressive symptoms, and cognitive function remain unclear. Prior literature has primarily focused on the association between a single physical disease (e.g., diabetes) or specific disease clusters (e.g., cardiometabolic conditions) and cognitive impairment, while other researchers have separately analyzed the effects of mental health issues like depression on physical multimorbidity or individual cognitive function [8-9]. Few studies have examined the combined effects of physical and mental illnesses on brain health, and the extent to which depressive symptoms may modify the association between physical multimorbidity and cognitive function remains uncertain [9-10]. Furthermore, relevant research has predominantly been conducted in high-income countries with relatively rich health data resources [11-12], with limited evidence from middle- and low-income countries.

This study aims to investigate the relationship between mental-physical multimorbidity and cognitive decline in three middle- and low-income countries—China, India, and Indonesia—to provide additional evidence for policy development.

1. Data and Methods

1.1 Data Sources This study utilized three large-scale, nationally representative population survey datasets: the China Health and Retirement Longitudinal Study (CHARLS), the Longitudinal Aging Study in India (LASI), and the Indonesian Family Life Survey (IFLS). The analysis adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [13].

The primary rationale for selecting China, India, and Indonesia stems from the limited research evidence from middle- and low-income countries and the innovative value of conducting comparative analyses across multiple nations. These three countries represent large-population developing nations in Asia with substantial sample sizes, rich measurement indicators, and high data quality.

CHARLS is a nationally representative survey providing information on health and socioeconomic status among Chinese adults aged 45 and older [14]. This study analyzed data from 14,705 participants in the third wave (2015), which included blood tests, physical examinations, and responses to cognitive and depression items. Although later CHARLS datasets are available, the third wave offered more comprehensive data.

LASI is India' s largest and most comprehensive aging survey, with the first wave (2017–2018) collecting health and healthcare utilization information from 72,250 adults aged 45 and older and their spouses through multistage probability

sampling. This study used data from 59,762 participants who completed the cognitive function section and health measurements [15].

IFLS is Indonesia' s only large-scale longitudinal survey. The original sampling frame covered 13 of 27 provinces. This study used the fifth wave (2014–2015), which included 9,196 participants aged 45 and older who completed Book B sections on chronic diseases and cognitive function [16].

After combining samples from the three countries and excluding those with missing values (<10%), the final analytical sample comprised 73,119 respondents, including 9,951 from CHARLS, 54,802 from LASI, and 8,446 from IFLS.

1.2 Cognitive Function Assessment All three surveys included three key domains to reflect cognitive function levels: time orientation, word recall, and numeracy. Specific items are detailed in the supplementary table (available via QR code). Time orientation questions primarily included date and day of the week, with each correct answer scoring 2 points (CHARLS also assessed month and year, with 4 questions totaling 4 points). Word memory comprised immediate and delayed recall sections. Four lists each contained 10 nouns randomly assigned to participants. Participants were asked to immediately recall as many nouns as possible and then recall them again after completing other survey questions (delayed recall). The total word recall score ranged from 0 to 20. In the numeracy test, participants were asked to subtract 7 from 100 sequentially five times, with scores ranging from 0 to 5. This study converted raw scores from each module to standardized scores (z-scores) using the mean and standard deviation (s) for each domain. The average of the three standardized scores was then rescaled to a 0–100 range, with higher scores indicating better cognitive function.

1.3 Mental-Physical Multimorbidity Definition Mental-physical multimorbidity was specifically defined as the coexistence of two or more physical chronic diseases accompanied by depressive symptoms. The three datasets assessed common chronic conditions and symptoms to the extent possible. Seven self-reported chronic non-communicable diseases consistently measured across datasets were selected: hypertension, diabetes, asthma/chronic lung disease, heart attack/coronary heart disease, stroke, cancer, and arthritis. The presence of physical chronic disease was determined based on responses to the question, "Has a medical professional diagnosed you with the following conditions?" In addition to self-reported measures, hypertension was also identified through three measurements of systolic and diastolic blood pressure using an electronic sphygmomanometer during physical examinations. Participants with mean measured systolic blood pressure $ $140 mmHg (1 mmHg=0.133 kPa) and/or diastolic blood pressure $ $90 mmHg, or those self-reporting a physician diagnosis of hypertension, were classified as having hypertension.

The total number of chronic non-communicable diseases per participant was summed (range: 0–7) and categorized as: no chronic disease, single chronic

disease, or two or more chronic diseases (multimorbidity). Depressive symptoms were assessed using self-reported questions and the 10-item version of the Center for Epidemiologic Studies Depression Scale (CES-D-10) [17]. Participants responded to eight positive statements and two negative statements using a 4-point Likert scale: rarely, a few days (1–2 days/week), occasionally (3–4 days/week), or most of the time (5–7 days/week). Negative statements were scored from 0 (rarely) to 3 (most of the time), while positive statements were reverse-scored from 3 (rarely) to 0 (most of the time). Total scores ranged from 0 to 30. Respondents who reported a health professional diagnosis of depression or had a CES-D-10 score $ $10 were classified as having depressive symptoms.

Based on the number of chronic non-communicable diseases and the presence of depressive symptoms, five categories of mental-physical multimorbidity were constructed: (1) no chronic disease (no physical chronic disease, no depressive symptoms); (2) single chronic disease (one physical chronic disease, no depressive symptoms); (3) physical multimorbidity (two or more physical chronic diseases, no depressive symptoms); (4) depressive symptoms only (no physical chronic disease, with depressive symptoms); and (5) mental-physical multimorbidity (two or more chronic diseases with depressive symptoms).

1.4 Covariates Covariates included sex (male, female), age (45–49, 50–59, 60–69, $ 70*years*), *maritalstatus*(*unmarried*, *married*), *educationlevel*(*none*, *primary*, *secondary*, *highschoolland*
Per capita household consumption expenditure (PCE) was used as a socioeconomic status indicator, divided into five equal groups from Q1 (lowest) to Q5 (highest). Country-specific variables such as ethnicity (Indonesia) and caste (India), as well as alcohol consumption status (China and India), were also included in descriptive statistics and regression models.

1.5 Statistical Methods Statistical analysis was performed using STATA 17.0 and Excel software. The study described sample characteristics and cognitive function scores across the three surveys, presenting normally distributed continuous data as mean ± standard deviation ($\bar{x}$±s). Multivariable linear regression models were used to examine the overall association between physical multimorbidity, depressive status, and cognitive function, adjusting for covariates described in section 1.4. Based on the overall analysis, stratified analyses by sex and residence were further conducted, using participants without chronic disease as the reference group. Results are reported as regression coefficients (β) and 95% confidence intervals (CI). Statistical significance was set at P<0.05.

2. Results

2.1 Sample Characteristics and Cognitive Function Scores Among the 9,951 Chinese respondents, 4,884 (49.3%) were male and 5,067 (50.7%) were female; the majority were aged 50–59 years (35.6%, 3,601/9,951), with a mean cognitive function score of (54.7$±19.9).*Amongthe*54, 802*Indianrespondents*, 26, 048(47.3±20.0).*Amongthe*8, 446
Detailed characteristics and cognitive function scores are presented in Table 1 .

2.2 Association Between Mental-Physical Multimorbidity and Cognitive Function Multivariable linear regression analysis, using cognitive function scores as the dependent variable (continuous) and mental-physical multimorbidity status as the independent variable, adjusted for sex, age, marital status, ethnicity, caste, education level, household economic status, employment, residence, smoking, alcohol consumption, and BMI, revealed the following:

In China, respondents with mental-physical multimorbidity (β=-6.99, 95%CI=-8.26~-5.71) and those with depressive symptoms only (β=-4.59, 95%CI=-6.29~-2.90) had significantly lower cognitive function than those without chronic disease ($P<0.05$). In India, respondents with mental-physical multimorbidity (β=-2.76, 95%CI=-3.41~-2.11) and those with depressive symptoms only (β=-2.13, 95%CI=-2.84~-1.43) had significantly lower cognitive function than those without chronic disease ($P<0.05$). In Indonesia, respondents with mental-physical multimorbidity (β=-2.75, 95%CI=-4.10~-1.41) and those with depressive symptoms only (β=-2.20, 95%CI=-3.82~-0.57) had significantly lower cognitive function than those without chronic disease ($P<0.05$). Results are detailed in Table 2 .

2.3 Gender-Stratified Analysis Further gender-stratified analysis using the same variable specifications showed that in China, both males and females with depressive symptoms only and those with mental-physical multimorbidity had significantly lower cognitive function than their counterparts without chronic disease ($P<0.05$). In India, both males and females with depressive symptoms only and those with mental-physical multimorbidity had significantly lower cognitive function than those without chronic disease ($P<0.05$). In Indonesia, males with physical multimorbidity, depressive symptoms only, and mental-physical multimorbidity had significantly lower cognitive function than males without chronic disease ($P<0.05$), while females with mental-physical multimorbidity had significantly lower cognitive function than females without chronic disease ($P<0.05$). Results are presented in Table 3 .

2.4 Residence-Stratified Analysis Residence-stratified analysis revealed that in China, urban residents with mental-physical multimorbidity had significantly lower cognitive function than urban residents without chronic disease ($P<0.05$), while rural residents with depressive symptoms only and mental-physical multimorbidity had significantly lower cognitive function than rural residents without chronic disease ($P<0.05$). In India, both urban and rural residents with depressive symptoms only and mental-physical multimorbidity had significantly lower cognitive function than their counterparts without chronic disease ($P<0.05$). In Indonesia, urban residents with depressive symptoms only and mental-physical multimorbidity had significantly lower cognitive function than urban residents without chronic disease ($P<0.05$). Results are detailed in Table 4 .

3. Discussion

This study utilized nationally representative samples from three major developing countries—China, India, and Indonesia. Despite varying degrees of population aging across these nations, the findings consistently demonstrated that mental-physical multimorbidity and depressive symptoms were significantly associated with lower cognitive function among middle-aged and older adults. These results align with previous studies conducted in middle- and high-income countries [3,7-10], suggesting that mental-physical multimorbidity may contribute to cognitive decline. The prevalence of physical multimorbidity was higher among Chinese older adults compared to those in India and Indonesia, while mental-physical multimorbidity was more common among Indian residents. In developing countries, particularly those experiencing pronounced population aging, greater attention should be paid to residents' mental health and the cognitive impairment risks associated with coexisting physical and mental diseases.

Across the three country samples, female sex, older age, lower education, lower household income, unemployment, and rural residence emerged as potential risk factors for cognitive decline, consistent with findings from studies in the United States, Japan, and India [18-20]. UK survey data have also identified social engagement, sleep duration, and dietary habits as major influences on cognitive function [21]. Jennings et al. [22] compared data from adults aged 50 and older in the United States, South Africa, Mexico, and China, revealing that marital status played an important role in cognitive function for both men and women.

As the widespread impact and challenges of chronic disease multimorbidity become increasingly severe, healthcare systems and financing mechanisms in many developing countries must transition from a single-disease model to a new multimorbidity care model. This shift should incorporate not only physical diseases but also gradually integrate mental health promotion into new multimorbidity management models and payment systems. Strengthening integration across different types of healthcare and improving comprehensive disease diagnosis and treatment quality are essential for more effective chronic disease multimorbidity management [23]. Domestic studies have attempted to evaluate the effectiveness of "people-centered integrated care" initiatives launched in Shanghai and Shenzhen, which encourage primary healthcare institutions to manage patients with multiple chronic conditions. However, evaluation results have been inconsistent, with significant quality improvements observed in Shanghai but not in Shenzhen [24]. The Indian government has also launched the National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS). The 2013 National Action Plan and Monitoring Framework for non-communicable disease prevention and control further revised program strategies and implementation [26], comprehensively addressing future challenges posed by mental and physical diseases. However, for most developing countries and regions, innovative management models for mental-physical multimorbidity remain limited, and scientific intervention designs and effectiveness evaluations

are lacking.

This study carries important public health and policy implications for cognitive health promotion and mental-physical multimorbidity risk prevention among middle-aged and older populations. Healthcare service delivery and system efficiency in developing countries have not reached optimal levels [27]. Resource-limited countries and regions urgently need targeted strategies to address the growing burden of aging, chronic disease multimorbidity, and mental health issues, which are also important risk factors for cognitive impairment and dementia [28,29]. Clinicians, psychiatrists, and general practitioners should recognize that cognitive decline is highly prevalent among patients with mental-physical multimorbidity. Future screening for depressive symptoms among patients with physical diseases is recommended to prevent cognitive decline [12]. Primary healthcare assessments of patient mental health should also include basic information such as pain, illness, discomfort, hunger, loneliness, boredom, lack of intimate relationships, and worries [30]. Additionally, adopting a life-course perspective and interdisciplinary, multi-sectoral collaborative approaches that encourage community participation are crucial for preventing cognitive impairment [30-33]. This study also suggests that policymakers should pay greater attention to vulnerable populations by expanding the scope of disease coverage under China' s urban-rural basic medical insurance and critical illness insurance programs, improving India' s National Health Protection Scheme and Indonesia' s National Health Insurance Program to enhance screening and management of multimorbidity and mental health problems, and strengthening financial risk protection for disadvantaged groups [34-37]. Countries should also leverage comparative advantages to accumulate patient-centered mental-physical multimorbidity management experience and improve health governance and equity.

This study has several limitations. First, the use of cross-country measures for mental and physical health may involve conceptualization differences across ethnic and cultural groups, a common challenge in multinational comparative studies. Interpretation and inference from the results should therefore be approached with caution. Second, self-reported chronic disease status may involve recall bias, and the number and categories of chronic diseases included were limited. Third, the lack of longitudinal data for some countries (e.g., LASI) prevented longitudinal analysis, and the cross-sectional design limits causal inference. Finally, uneven healthcare resources and health literacy in developing countries result in varying chronic disease awareness rates among participants and potential disease underestimation. Future research should employ more consistent disease measurement and diagnostic tools and conduct longitudinal studies with long-term follow-up among populations at risk for cognitive decline.

In conclusion, this three-country analysis demonstrates that cognitive decline is highly prevalent among older adults with depressive symptoms and mental-physical multimorbidity, particularly in populous developing countries facing substantial aging burdens. The findings advocate for establishing a patient-centered integrated healthcare and service delivery model to enhance preven-

tion and management efficiency for mental-physical multimorbidity of chronic non-communicable diseases and depressive symptoms, with regular depression screening, especially among patients with chronic disease multimorbidity, to prevent cognitive decline and delay dementia onset.

Author Contributions: ZHAO Siqi, YE Xing, and HAN Li conceptualized and designed the study and drafted the manuscript. ZHAO Yang, Kanya Anindya, Tiara Marthias, and Mercian Daniel performed data collation, statistical analysis, and interpretation. ZHAO Siqi and ZHAO Tianhao conducted literature searches and organization. ZHAO Siqi, ZHAO Yang, and ZHAO Tianhao revised the initial draft. HAN Li supervised quality control and is responsible for the overall content.

Conflict of Interest: The authors declare no conflicts of interest.

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