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Differential Associations Between Depressive Symptom-Domains With Anxiety, Loneliness, and Cognition in a Sample of Community Older Chinese Adults: A Multiple Indicators Multiple Causes Approach

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Abstract

Background and Objectives: Depressive symptoms are common in older adults, and often co-occur with other mental health problems. However, knowledge about depressive symptom-domains and their associations with other conditions is limited. This study examined depressive symptom-domains and associations with anxiety, cognition, and loneliness.

Research Design and Methods: A sample of 3,795 participants aged 60 years and older were recruited from the community in Hong Kong. They were assessed for depressive symptoms (Patient Health Questionnaire-9 [PHQ-9]), anxiety (Generalized Anxiety Disorder 7-item), loneliness (UCLA 3-item), and cognition (Montreal Cognitive Assessment 5-Minute Protocol). Summary descriptive statistics were calculated, followed by confirmatory factor analysis of PHQ-9. Multiple Indicators Multiple Causes analysis was used to examine the associations between mental health conditions in the general sample and subgroups based on depressive symptom severity.

Results: A 4-factor model based on the Research Domain Criteria showed the best model fit of PHQ-9 (χ^2/df = 10.63, Root-Mean-Square Error of Approximation = 0.05, Comparative Fit Index = 0.96, Tucker–Lewis Index = 0.93). After adjusting for demographics, 4 depressive symptom-domains were differentially associated with anxiety, loneliness, and cognition across different depression severity groups. The Negative Valance Systems and Internalizing domain (*NVS-I*; guilt and self-harm) were consistently associated with anxiety (β = 0.45, 0.44) and loneliness (β = 0.11, 0.27) regardless of depression severity (at risk/mild vs moderate and more severe, respectively, all $p < .001$).

Discussion and Implications: The consistent associations between the *NVS-I* domain of depression with anxiety and loneliness warrant attention. Simultaneous considerations of depressive symptom-domains and symptom severity are needed for designing more personalized care.

Clinical Trials Registration Number: NCT03593889

Translational Significance: Depressive symptoms are common in older adults and are heterogeneous with multiple symptom-domains. This study investigated depressive symptom-domains among community-dwelling older Chinese in Hong Kong, and examined their association with anxiety, loneliness, and cognition. We found four depressive symptom-domains in this sample, and people with different depressive symptom-domains have differential possibilities to demonstrate co-occurrent anxiety, loneliness, and cognitive decline. Those with feelings of inappropriate guilt and suicidal ideation were more likely to show anxiety symptoms and loneliness as well. A more fine-grained assessment of depression is needed for personalized care.

Keywords: Common mental health issues, Depression and anxiety, Mental health, Quantitative research methods, Research domain criteria

Depression is a common mental health condition in older people with a global prevalence of 13.3% (95% confidence interval: 8.4%–20.3%; Abdoli et al., 2021), and it is associated with a high rate of mortality and a significant risk of dementia

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(Baldwin et al., 2006). The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), describes nine major depressive disorder (MDD) symptoms, including (1) anhedonia, (2) depressive mood, (3) sleep difficulties, (4) fatigue, (5) appetite/weight symptoms, (6) feelings of inappropriate guilt/worthlessness, (7) diminished concentration, (8) psychomotor problems, and (9) self-harm/suicidal ideation (American Psychiatric Association, 2013). The diagnostic criteria of MDD concern not only the number of symptoms but also frequency, duration, and/or severity, reflecting the conceptualization of depression along a spectrum, with increasing severity varying from nonsymptomatic to showing subclinical symptoms to having MDD (Ayuso-Mateos et al., 2010). Although the causes and very nature of depression remain subject to debate, it is widely acknowledged that depression is a heterogeneous condition with multiple symptom-domains and subtypes, and two persons with an MDD diagnosis may share no single symptom (Chen et al., 2000; Fried & Nesse, 2015). People may experience depressive symptoms but fall short of the diagnostic threshold for MDD, and among them, the depressive symptoms may also present in heterogeneous patterns (Chen et al., 2000).

Prevention of Depression in Subclinical and At-Risk Populations

Traditionally, research and intervention for depression have focused on the clinical population, but more efforts have been devoted to the reduction of symptoms and risk factors because numerous studies have documented the benefits of early intervention and prevention of depression in subclinical and at-risk populations (Cuijpers et al., 2014; Rebar et al., 2015). Subclinical, or subthreshold, depression is when an individual displays clinically relevant, that is, moderate and more severe, depressive symptoms, but standard diagnostic criteria are not met (Rodríguez et al., 2012). It is more prevalent than MDD in the community, associated with increased risk for MDD, decreased health-related quality of life, and mortality rates in older people (Chachamovich et al., 2008; Cuijpers et al., 2013; Lee et al., 2019). Even without clinically relevant depressive symptoms, older adults face multiple risk factors for depression, including biological (chronic health condition, cognitive impairment, and functional limitations), psychological (external locus of control, dysfunctional coping, negative self-image, and psychopathology), and social factors (smaller network size, stressful events, and living alone; Vink et al., 2008). Following stressful events such as retirement, death of loved ones, and functional decline, it is common for older people to develop depressive symptoms such as sleep disturbance, loss of interest, and depressed mood (Maier et al., 2021).

Increasing evidence supports differential preventive strategies for mental health in at-risk/with mild depressive symptoms and subclinical populations. Selective prevention is effective in promoting mental well-being and preventing mental disorders in those at-risk or with mild symptoms, and indicated prevention is effective in shifting the trajectories toward less debilitating outcomes or delaying the onset of mental disorders among those with moderate and more severe depressive symptoms (Arango et al., 2018). In the case of late-life depression, selective prevention focuses on people with established susceptibility based on risk factors such as social isolation and bereavement, where group-based psychoeducation and behavioral activation approaches are typically used, and indicated prevention focuses on those already living with clinically relevant symptoms, where more targeted intervention is prescribed (Almeida, 2014; Reynolds et al., 2012). These strategies have proven effective and cost-effective, and given the trend of population aging and the shortage of the mental health workforce, it is crucial to develop more targeted and cost-effective risk-reduction strategies for different populations (Reynolds et al., 2012).

Depressive Symptom-Domains

The Patient Health Questionnaire-9 (PHQ-9) is one of the depression screening instruments comprising items that map onto the DSM diagnostic criteria for depressive symptoms (Kroenke et al., 2001). Some studies using the PHQ-9 provided support for one single underlying factor of depressive symptoms (Cameron et al., 2008; Keum et al., 2018); however, many more studies suggested multiple domains of depressive symptoms detectable by the PHQ-9, mostly two-factor structure (cognitive–affective and somatic; Chilcot et al., 2013; Petersen et al., 2015).

Despite the utility of the DSM, it may not reflect the recent advances in understanding mental disorders based on behavioral dimensions and neurobiological measures (Dillon et al., 2014). To address this limitation, the National Institute of Mental Health launched the Research Domain Criteria (RDoC) initiative to provide a new framework for psychopathology research rooted in a dimensional approach to mental health (Insel et al., 2010). A recent study drew on the RDoC matrix and used factor and qualitative analysis to map the PHQ-9 items, and identified a four-factor model: Negative Valence Systems and Externalizing (*NVS-E*; anhedonia and depression), Negative Valence Systems and Internalizing (*NVS-I*; guilt and self-harm), Arousal and Regulatory Systems (*ARS*; sleep, fatigue, and appetite), and Cognitive and Sensorimotor Systems (*CSS*; concentration and psychomotor); the authors suggested that recognizing these phenotypes may provide a step toward developing more personalized care depending on varying patterns of depressive symptoms (Gunzler et al., 2020).

Associations With Anxiety, Loneliness, and Cognition

There are abundant empirical research and theories on the associations between depressive symptoms and other mental health conditions in older adults. Among the common mental health issues in older people, this study focused on anxiety, loneliness, and cognition because these three conditions have high rates of coexistence or complex relationship with depressive symptoms, are preventable or manageable if identified early, and would lead to worse mental health outcomes and lower quality of life if left untreated (Cacioppo et al., 2006; Kalin, 2020; Kaup et al., 2016).

Many studies focused on associations between two conditions. For depression and anxiety, a worldwide survey reported that 45.7% of individuals with lifetime depression had a history of one or more anxiety disorders (Kessler et al., 2015), and a review suggested that the high co-occurrence may be due to shared structural and functional brain alterations in circuits involving emotion regulation and cognitive control (Kalin, 2020). For depressive symptoms and loneliness, a longitudinal study

revealed reciprocal influences between loneliness and depressive symptomatology, signaling a synergistic effect of depressive symptoms and loneliness to diminish well-being in older adults (Cacioppo et al., 2006). For depressive symptoms and cognition, the relationship is complex; some studies indicated that depressive symptoms are risk factors for cognitive decline or dementia (Byers & Yaffe, 2011); some suggested that older adults may develop depressive symptoms in reaction to cognitive decline (Jajodia & Borders, 2011); and others theorized that both conditions might reflect a similar neurodegenerative process (Panza et al., 2010).

Research in the recent two decades is taking a more holistic approach to examine the complex associations between more than two mental health issues, for understanding the complex mental health needs of older people may help tailor integrated and personalized interventions. Among these studies, cognition is often the central focus, and much attention is given to improving or maintaining cognitive health. For example, one study examined the association of anxiety, depression, and worry symptoms on cognitive performance in older adults and found that worry symptoms had the highest contribution in predicting cognition; in contrast, anxiety and depressive symptoms had few unique associations with cognitive performance (de Vito et al., 2019). Another study examined the behavioral mechanisms between loneliness, depression, and cognition and found that loneliness and depression may associate with fewer health-promoting and cognitive-stimulating behaviors, for example, fewer physical, social, and cognitive activities, leading to cognitive impairment according to the "use it or lose it" hypothesis (Salthouse, 2006).

In summary, depressive symptoms are heterogeneous and with multiple domains, and they are associated with other preventable or manageable mental health conditions in older adults. So far, despite abundant research on the associations between depression, anxiety, loneliness, and cognition in older people, depression took less of a central focus; little is known about the depressive symptom-domains in older people and whether and how different symptom domains are associated with other mental health conditions in a community sample. It is also of clinical relevance to differentiate the relationships between these mental health conditions in predominately healthy but with some risks or mild symptoms and in subclinical populations with moderate and more severe symptoms, because the related management strategies of depressive symptoms also differ for these two populations (Kok & Reynolds, 2017). Characterizing depressive symptom-domains and their associations with other common mental health conditions in different depressive symptom severity groups among older people may improve diagnostic accuracy and inform more personalized care planning. The aims of the present study were threefold: (1) to examine the depressive symptom-domains, (2) to investigate the associations between depressive symptom-domains and other common mental health conditions, including anxiety, loneliness, and cognition, and (3) to compare the associations between at-risk population and subclinical population in community-dwelling older adults in Hong Kong.

Method

Participants

Participants were community-dwelling older adults at risk of depression or with subclinical depressive symptoms who participated in a collaborative stepped care with peer support program offered by nongovernmental organizations (NGOs) in Hong Kong, registered with ClinicalTrials.gov (NCT03593889; Liu et al., 2022). The inclusion criteria of this study were (1) aged 60 years or older; (2) at risk for depression, defined as had no depressive symptoms (PHQ-9 total score <5) but at least one risk factor of late-life depression, including reported loneliness, lack of social interaction, lack of meaningful or enjoyable daily activities, chronic pain, more than four common chronic diseases and/or recent bereavement; or (3) had mild to moderately severe depressive symptoms (5 < PHQ-9 total score < 20). The exclusion criteria were (1) known history of autism, intellectual disability, schizophrenia spectrum disorder, bipolar disorder, Parkinson's disease, or dementia/significant cognitive impairment; (2) significant suicidal risk measured using PHQ-9 item 9 (self-harm/suicidal ideation), and follow-up risk assessment; and (3) declined to participate or difficulty in communication. The analysis used screening data for admission to the program collected by trained social workers between January 2018 and September 2019 from 3,795 community-dwelling older adults. Written informed consent was obtained from all participants.

Measures

Depressive symptoms were measured using the validated Chinese version of the PHQ-9, which has a high internal consistency (Cronbach's $\alpha = 0.91$; Yeung et al., 2008). Responses to each item in the PHQ-9 are rated on a 4-point Likert scale from 0 (not at all) to 3 (nearly every day). The total score of the PHQ-9 ranges from 0 to 27, with a higher score representing a more severe degree of depression. A classification system is commonly used to interpret PHQ-9 score, with a predefined cutoff score of 10 as a dichotomous scoring system for differentiating clinically relevant depressive symptoms (Kroenke et al., 2001). Because this study used a community sample with no depression diagnosis, we categorized those who scored 0–9 on the PHQ-9 as the "at-risk/mild" and those who scored 10 and above as "moderate and more severe" depressive symptom groups. This categorization has service implications because the corresponding preventive care approaches could differ for these two groups.

Anxiety was measured by the Chinese version of the seven-item Generalized Anxiety Disorder (GAD-7) questionnaire, which has a good internal consistency (Cronbach's $\alpha = 0.89$; Tong et al., 2016). Each item is rated on a 4-point Likert scale from 0 (not at all) to 3 (nearly every day), the total score ranges from 0 to 21, and a higher score indicates more severe depressive symptoms (Spitzer et al., 2006).

Loneliness was measured by the locally adapted three-item UCLA Loneliness Scale (UCLA-3) with a high internal consistency (Cronbach's $\alpha = 0.87$; Liu et al., 2020). It consists of three items: lack of companionship, feeling left out, and isolated over the past 2 weeks. The locally adapted Chinese version has four possible responses for each item from 0 (never) to 3 (often). The total score ranges from 0 to 9 points, with a higher score indicating a higher degree of perceived loneliness (Hughes et al., 2004).

Cognition was measured by the Chinese version of the Montreal Cognitive Assessment 5-minute protocol (MoCA-5), which has an acceptable level of reliability (Cronbach's $\alpha = 0.79$) (Wong et al., 2015). Five domains were tested: attention, verbal learning and memory, executive function, language,

and orientation. The sum score of the MoCA-5 ranges from 0 to 30, with a higher score indicating better cognitive function.

Participants' demographic characteristics, including age (years), sex (male or female), education level (highest attainment), marital status (married/cohabit or otherwise), and living arrangement (living alone or otherwise), were also collected.

Data Analysis

First, descriptive statistics were used to summarize demographic variables and responses to clinical measures. Little's Missing Completely at Random test was conducted to identify the mechanism of missing data (Newgard & Haukoos, 2007). Results suggested that data were probably not missing at random; missing data patterns and handling procedures are reported in Supplementary Table 1. Multiple imputations were, therefore, used to handle the missing data (Sterne et al., 2009). Second, the internal consistencies of the PHQ-9, GAD-7, UCLA-3, and MoCA-5 were evaluated using Cronbach's alpha. Third, confirmatory factor analyses (CFA) were conducted to test and compare three depressive symptom-domain models derived from the literature: single-factor, two-factor (somatic and cognitive–affective), and four-factor model mapped onto RDoC.

After evaluating the measurement model with CFA, we used the Multiple Indicators Multiple Causes (MIMIC) model to measure the associations of depressive symptom-domains with anxiety, loneliness, and cognitive function. The MIMIC model is a specific application of Structural Equation Model (SEM) that involves latent variables with usual multiple indicators, and are simultaneously predicted by observed variables (Jöreskog & Goldberger, 1975). Compared with traditional SEM, a MIMIC model allows the simultaneous evaluation of the effect of the covariates on the factor indicators, providing a better insight into the relations between measured items, latent variables, and covariates. Three MIMIC models were tested: a general model of the total sample and two models by depression severity groups. The model fit of the CFA and MIMIC models was determined with the following commonly used indicators: chi-square (χ^2)/degree of freedom (*df*) ratio, comparative fit index (CFI), Tucker–Lewis index (TLI), goodness-of-fit index (GFI), the standardized root-mean-square residual (SRMR) and a noncentrality-based index, the root-mean-square error of approximation (RMSEA). The usual rule of thumb for model fit indices is that χ^2/df equals or below 5; CFI, TLI, and GFI values greater than 0.90; and SRMR and RMSEA values below 0.08 indicate an acceptable fit (Marsh & Hocevar, 1985), while χ^2/df equals or below 2; CFI, TLI, and GFI values greater than 0.95; and SRMR and RMSEA below 0.06 indicate good model fit (Hu & Bentler, 1999). Supplementary Table 1 summarizes the details of the statistical analyses and results. Sensitivity analyses using nonimputed data were performed and reported in Supplementary Tables 2 and 3. Statistical analyses were conducted using SPSS (24.0) and AMOS (24.0) statistical software.

Ethics Statement

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human subjects/patients were approved by the Human Research Ethics Committee (HREC) of the University of Hong Kong.

Results

Descriptive Statistics

Table 1 shows the sample's descriptive statistics (N = 3,795) and the missing value pattern of each variable. The total percentage of missing data was 8.48%, with the highest missing rate of 4.91% in MoCA scores, and missing data were addressed using multiple imputations (Supplementary Table 1). Participants had a mean age of 77.34 years (standard deviation [*SD*] = 8.74), and most were female (77.60%). They scored 4.43 (*SD* = 4.57) on the GAD-7, 3.98 (*SD* = 2.96) on the UCLA-3, 20.56 (*SD* = 5.32) on the MoCA-5, and 6.44 (*SD* = 4.00) on the PHQ-9 on average. In terms of responses to individual items of the PHQ-9, symptoms having a relatively higher score were sleep problems (*Mean* = 1.40, *SD* = 1.04), fatigue (*Mean* =1.21, *SD* = 0.92), and depressed mood (*Mean* = 1.07, *SD* = 0.92); the average scores of all other symptoms were lower than one. We separated the analyses by depression severity (at risk/mild [PHQ-9 ≤ 9] vs moderate and more severe [PHQ-9 ≥ 10]) and compared the two groups; results are summarized in Table 1.

CFA of the PHQ-9

Reliability analyses suggested that all measures had satisfactory to good internal consistency (PHQ-9: Cronbach's α = 0.70; GAD-7: 0.90; UCLA-3: 0.88; MoCA-5: 0.62; Tavakol & Dennick, 2011). Table 2 shows the factor loadings and model-fitting indices of four proposed PHQ-9 symptom-domains. Compared with the other two models, the four-factor model based on RDoC had the best model fit to the observed data (χ^2/df = 10.63, SRMR = 0.02, RMSEA = 0.05, GFI = 0.99, CFI = 0.96, TLI = 0.93), and the correlations between the four factors ranged between 0.62 and 0.78 (Figure 1). Although the relative chi-square is larger than 5, likely to be driven by the large sample size, all other model-fitting indices suggest good model fitting. Sensitivity analyses with original (nonimputed) data revealed similar results that the four-factor model based on RDoC had the best model fit (χ^2/df = 9.24, SRMR = 0.03, RMSEA = 0.05, GFI = 0.99, CFI = 0.96, TLI = 0.93).

MIMIC Models

Table 3 shows the regression weights between clinical variables and model-fitting indices of three MIMIC models; Figure 2 summarizes the standardized regression weights of significant associations between key variables under examination (see Supplementary Figure 1 for details concerning all variables). The results of Model 1 with the overall sample suggested acceptable model fitting (χ^2/df = 6.68, SRMR = 0.02, RMSEA = 0.04, GFI = 0.99, CFI = 0.97, TLI = 0.92). Among the basic demographics, only education level had a negative association with the *NVS-I* domain (β = –0.07), and others had no association with any depressive symptom-domain. Anxiety (GAD-7) showed a positive association with all four domains (all $p < .001$), among which the strongest was with the *CSS* domain (β = 0.63). Loneliness (UCLA-3) was positively related to three symptom-domains (all $p < .001$) but not the *ARS*. Note that living alone and loneliness were not related, nor was living alone associated with any depressive symptom-domain, suggesting that subjective appraisal of

Table 1. Basic and Clinical Characteristics of Participants

Variable[a]	Overall (*n* = 3,795)	Subgroups based on depressive symptoms severity		
		At risk/mild (PHQ-9 0–9) (*n*= 3,146)	Moderate and more severe (PHQ-9 ≥10) (*n* = 649)	*t*/χ^2
Age, mean (*SD*), years	77.34 (8.74)	77.52 (8.72)	76.48 (8.81)	–2.77***
Sex, female, *n* (%)	2,946 (77.60)	2,436 (77.40)	510 (78.60)	0.38
Married/cohabit, *n* (%)	1,497 (39.90)	1,264 (40.18)	233 (35.91)	22.86***
Education, level, *n* (%)				
No formal education	1,089 (28.70)	901 (28.64)	188 (28.97)	11.00
Bok Bok Zaai[b]	189 (4.98)	167 (5.31)	22 (3.39)	
Primary school	1,404 (37.00)	1,153 (36.65)	251 (38.67)	
Middle school	555 (14.63)	477 (15.16)	78 (12.02)	
High school	351 (9.25)	291 (9.25)	60 (9.24)	
Diploma	64 (1.69)	48 (1.53)	16 (2.47)	
Bachelor's degree	59 (1.56)	49 (1.56)	10 (1.54)	
Living alone, *n* (%)	1,574 (41.48)	1,315 (41.80)	259 (39.91)	0.79
GAD-7 scores, mean (*SD*)	4.43 (4.57)	3.57 (3.87)	8.58 (5.35)	27.92***
UCLA-3 scores, mean (SD)	3.98 (2.96)	3.72 (2.88)	5.26 (3.00)	12.34***
MoCA-5 scores, mean (*SD*)	20.56 (5.32)	20.65 (5.23)	20.14 (5.73)	2.13*
PHQ-9 scores, mean (*SD*)	6.44 (4.00)	5.08 (2.60)	13.03 (2.94)	69.33***
Responses to PHQ-9 items				
1. Anhedonia	0.89 (0.92)	0.68 (0.77)	1.87 (0.95)	34.30***
2. Depressed mood	1.07 (0.92)	0.89 (0.83)	1.96 (0.82)	29.88***
3. Sleep	1.39 (1.04)	1.24 (1.00)	2.15 (0.92)	21.52***
4. Fatigue	1.20 (0.92)	1.03 (0.83)	2.06 (0.87)	28.54***
5. Appetite	0.26 (0.62)	0.14 (0.43)	0.81 (0.98)	27.67***
6. Guilt	0.52 (0.81)	0.31 (0.58)	1.53 (0.98)	42.69***
7. Concentration	0.65 (0.78)	0.52 (0.66)	1.25 (1.00)	23.07***
8. Psychomotor	0.25 (0.56)	0.16 (0.41)	0.68 (0.89)	22.93***
9. Self-harm	0.21 (0.52)	0.11 (0.33)	0.71 (0.86)	29.75***

Notes: GAD-7 = generalized anxiety disorder-7; MoCA-5 = Montreal Cognitive Assessment 5-minute protocol; PHQ-9 = patient health questionnaire-9; *SD* = standard deviation; UCLA-3 = UCLA 3-item loneliness scale.
[a]Missing data pattern of the variables are summarized in Supplementary Table 1.
[b]Bok Bok Zaai: 1–3 years informal education provided by private institutions in Cantonese-speaking regions, gradually disappearing since the New Culture Movement in China in the 1910s.
*$p < .05$. *** $p < .001$.

feeling lonely was conceptually different from living alone. Cognition (MoCA-5) was negatively associated with *NVS-E* (β = –0.17, $p < .001$) and *CSS* (β = –0.12, $p < .001$), but not *NVS-I* or *ARS* domains. Sensitivity analysis revealed similar results: the overall model fit was acceptable (χ^2/df = 6.18, SRMR = 0.02, RMSEA = 0.04, GFI = 0.99, CFI = 0.97, TLI = 0.93), anxiety was positively associated with all four domains, and cognition was negatively associated with *NVS-E* and *CSS* domains. The only difference was that loneliness was positively related to all four domains in the nonimputed sample, although the association with *ARS* domain was weak (β = 0.09, all $p < .05$).

In Model 2, with those at-risk or with mild depressive symptoms, the model fit indices indicated acceptable model fitting (χ^2/df = 6.34, SRMR = 0.03, RMSEA = 0.04, GFI = 0.99, CFI = 0.94, TLI = 0.86). Similar to the results of Model 1, anxiety (GAD-7) was positively associated with all four depressive symptom-domains (all $p < .001$), and the degrees of association were similar between those with *NVS-E* (β = 0.47), *NVS-I* (β = 0.45), and *CSS* (β = 0.45). Loneliness (UCLA-3) was positively associated with three symptom-domains (all $p < .001$) but not the *ARS*. Cognition (MoCA-5) had negative associations with *NVS-E* (β = –0.17, $p < .001$) and *CSS* (β = –0.34, $p < .001$). Sensitivity analysis results were similar: the overall model fit was slightly better (χ^2/df = 5.31, SRMR = 0.03, RMSEA = 0.04, GFI = 0.99, CFI = 0.96, TLI = 0.90), anxiety was positively associated with all four depressive symptom-domains, cognition with *NVS-E* and *CSS* domains; and the only difference was that loneliness was positively associated with all four domains as well, although the association with *ARS* domain was weak (β = 0.10, all $p < .05$).

In Model 3, with participants having moderate or more severe depressive symptoms, the model-fitting indices suggested good model fitting (χ^2/df = 1.04, SRMR = 0.03, RMSEA = 0.01, GFI = 0.99, CFI = 0.99, TLI = 0.99). Anxiety (GAD-7) was positively associated with *NVS-E* (β = 0.29), *NVS-I* (β = 0.44), and *CSS* (β = 0.60), all $p < .001$. Loneliness (UCLA-3) was only positively associated with *NVS-I* (β = 0.27, $p < .001$), but not other symptom-domains. Cognition (MoCA-5)

Table 2. Factor Loadings and Model-Fitting Indices of Three Theory-Based PHQ-9 Structures

Variable	Loadings	Model fit						
		χ^2/df	*p*	SRMR	RMSEA	GFI	CFI	TLI
One factor		563.48/27 = 20.87	<.001	0.03	0.07	0.97	0.89	0.85
Factor 1: Depression								
1. Anhedonia	0.61							
2. Depression	0.66							
3. Sleep	0.32							
4. Fatigue	0.43							
5. Appetite	0.37							
6. Guilt	0.61							
7. Concentration	0.40							
8. Psychomotor	0.33							
9. Self-harm	0.51							
Two factor		442.89/26 = 17.03	<.001	0.03	0.07	0.97	0.91	0.88
Factor 1: Somatic symptoms								
3. Sleep	0.44							
4. Fatigue	0.58							
5. Appetite	0.40							
Factor 2: Cognitive–affective symptoms								
1. Anhedonia	0.62							
2. Depression	0.67							
6. Guilt	0.61							
7. Concentration	0.40							
8. Psychomotor	0.33							
9. Self-harm	0.51							
Four factor		223.16/21 = 10.63	<.001	0.02	0.05	0.99	0.96	0.93
Factor 1: Negative valence systems and externalizing								
1. Anhedonia	0.67							
2. Depression	0.74							
Factor 2: Negative valence systems and internalizing								
6. Guilt	0.70							
9. Self-harm	0.57							
Factor 3: Arousal and regulatory systems								
3. Sleep	0.43							
4. Fatigue	0.58							
5. Appetite	0.41							
Factor 4: Cognitive and sensorimotor systems								
7. Concentration	0.44							
8. Psychomotor	0.38							

Notes: CFI = comparative fit index; *df* = degree of freedom; GFI = goodness-of-fit index; PHQ-9 = patient health questionnaire-9 items; RMSEA = root-mean-square error of approximation; SRMR = standardized root-mean -quare residual; TLI = Tucker–Lewis index.
[a]The criteria for a good model fit are: $\chi^2/df \leq 5.0$, SRMR < 0.0 8, RMSEA < 0.08, GFI > 0.90, CFI > 0.90, TLI > 0.90.

was not associated with any depressive symptom-domain. Sensitivity analysis again revealed similar results: the overall model fit was good (χ^2/df = 1.07, SRMR = 0.03, RMSEA = 0.01, GFI = 0.99, CFI = 0.99, TLI = 0.99); anxiety was positively and strongly associated with *NVS-E* and *NVS-I*, not with *ARS*; loneliness was only positively associated with *NVS-I*. The only differences were that anxiety was negatively and weakly with *CSS* (β = −0.16), same for cognition (β = −0.16, both $p < .05$).

Discussion

This study contributes to current knowledge by investigating the depressive symptom-domains and examining their associations with anxiety, loneliness, cognition, and demographic risk factors across groups with different depressive symptom severity. It is the first study of this kind to be conducted among community-dwelling older Chinese, and the results may have service implications as the symptom profiles derived from readily available measurements can help to inform

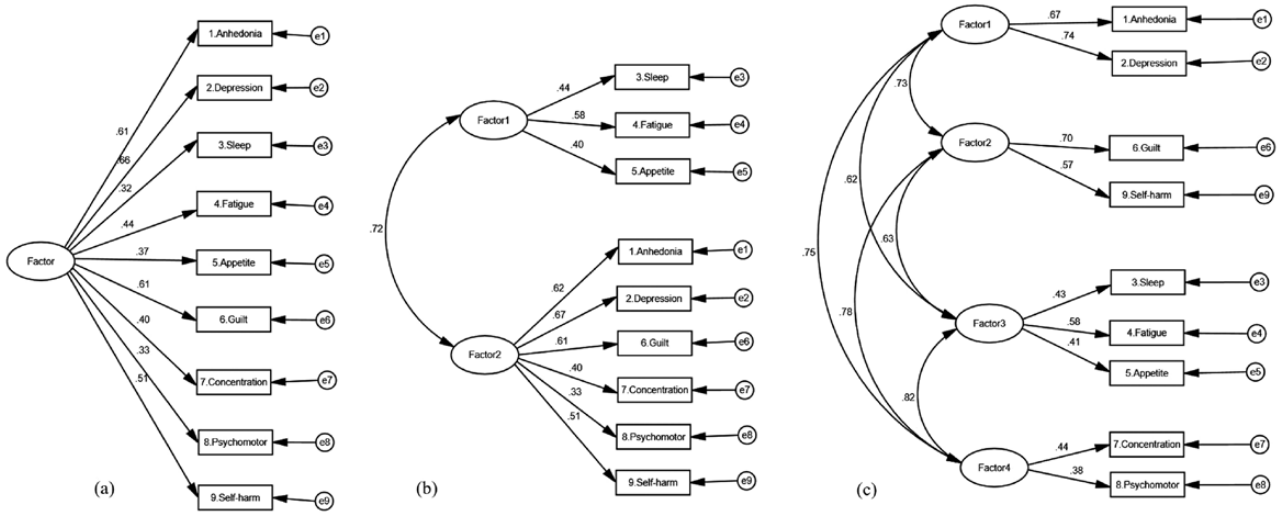

Figure 1. Confirmatory factor analysis (CFA) models of depression symptom-domains: (A) one factor, (B) two factor (somatic, cognitive–affective), and (C) four factor (based on Research Domain Criteria framework). Standardized regression weights were reported.

more personalized care. For older people in the community, screening for multiple mental health conditions is needed, and depressive symptom severity and symptom domains may be considered in service planning. Other than the well-established selective and indicated prevention for at-risk/mild symptom and subclinical groups, individuals with anhedonia and depressive mood are more likely to benefit from comprehensive preventive care such as group exercise, healthy lifestyle intervention, and active engagement in community affairs; and individuals with feelings of inappropriate guilt and self-harm thoughts may require more indicated prevention such as group compassion-focused therapy that improves self-esteem and peer group that builds social network.

First, our findings add evidence to the heterogeneity of depression in a community sample and support the four-factor structure of depression based on the RDoC framework (Gunzler et al., 2020). The high correlation between the four factors indicates that screening and monitoring the community population for depression using the total score of PHQ-9 is likely useful in most circumstances. However, monitoring different depressive symptom-domains must not be overlooked, as individuals with similar levels of depression severity may present with different symptom profiles. We found that community-dwelling older Chinese reported more symptoms in the *ARS* domain (sleep, fatigue, and appetite), which is consistent with the literature that older Chinese are more likely to somatize psychological distress or find it easier to express somatic complaints (Hybels et al., 2011). Therefore, it is important not to dismiss somatic complaints when assessing depression in older Chinese adults.

Second, we found that anxiety, loneliness, and cognition were differentially associated with depressive symptom-domains. In the overall sample, anxiety was positively associated with all four depressive domains, and the *CSS* domain (concentration and psychomotor) was mostly affected. It has been well documented that the comorbidity between anxiety and depression is high in older adults (Lamers et al., 2011). Our finding contributed to the literature that anxiety is more likely to affect the cognitive domain of depression than other domains. There are two plausible mechanisms to explain this association. For one, the attentional control theory proposes that individuals with an elevated level of anxiety would have attentional biases towards threatening stimuli, which may lead to difficulty filtering information from working memory and affect the monitoring of ongoing activities (Bar-Haim et al., 2007). Consequentially, the emotional information acquired from biased attention to threatening stimuli would be retained in thoughts and may lead to impaired concentration on other upcoming events (Eysenck et al., 2007). Alternative to the attentional control theory, anxiety could also be a psychological reaction to an individual's subjective cognitive decline, which could be an early manifestation of neurodegenerative disorders (Liew, 2020). A further cognitive examination may be needed for those exhibiting comorbid depression and anxiety to identify appropriate intervention approaches.

Loneliness was positively associated with three depressive symptom-domains, strongest in the *NVS-E* (anhedonia and depression), but not the *ARS* domain. The close association between loneliness and depression has been well established in older people (Lee et al., 2021), and our findings add to the literature that loneliness is more likely to affect the external negative valence system but less related to somatic domains of depression. Research has highlighted that older people are vulnerable to experiencing loneliness (Gardiner et al., 2020), and interventions to reduce loneliness could prevent or reduce depression in older adults (Fakoya et al., 2020). Assessing loneliness may also act as a screening tool to identify depression among older adults, especially in contexts with a more substantial stigma toward mental disorders (Liu et al., 2020).

Cognition was negatively associated with *NVS-E* and *CSS* but not the other two depressive symptom-domains. The significant association between global cognition assessed by MoCA-5 and *NVS-E* is consistent with one recent review on the commonalities between cognition, anhedonia, and brain insulin resistance, drawing from pathophysiological evidence (Hamer et al., 2019). Brain insulin resistance has long been hypothesized as the missing link between MDD and dementia, because of insulin's role in regulating cognitive function, dopamine function, reward, and emotional behavior (Kleinridders & Pothos, 2019). Besides pharmacotherapy that targets insulin signaling, exercise is effective in mitigating

Table 3. Regression Weights and Model-Fitting Indices of Three Multiple Indicators Multiple Causes (MIMIC) Models

Pathways		Model 1: Overall (N = 3,795)		Model 2: At-risk/mild (n = 3,146)		Model 3: Moderate and more severe (n = 649)	
		β	*SE*	β	*SE*	β	*SE*
Measurement model: Depressive symptom-domains							
NVS-E	Anhedonia	0.63***	0.02	0.49***	0.04	0.35***	0.20
	Depression	0.78***	0.04	0.77***	0.08	0.79***	0.49
NVS-I	Guilt	0.70***	0.03	0.46***	0.04	0.54***	0.09
	Self-harm	0.57***	0.02	0.46***	0.05	0.37***	0.10
ARS	Sleep	0.45***	0.03	0.36***	0.05	0.43***	0.21
	Fatigue	0.58***	0.06	0.55***	0.16	0.42**	0.32
	Appetite	0.40***	0.04	0.13***	0.04	−0.08	0.17
CSS	Concentration	0.44***	0.04	0.34***	0.04	0.24***	0.22
	Psychomotor	0.38***	0.04	0.10***	0.04	0.29***	0.30
Factor intercorrelations							
NVS-E	NVS-I	0.54***	0.01	0.29***	0.003	0.22*	0.01
	ARS	0.42***	0.01	0.03	0.004	−0.02	0.01
	CSS	0.47***	0.01	0.45***	0.004	−0.35	0.01
NVS-I	ARS	0.47***	0.01	−0.13*	0.01	−0.34*	0.02
	CSS	0.63***	0.01	−0.33*	0.01	0.05	0.02
ARS	CSS	0.76***	0.01	0.54***	0.01	−0.52	0.02
Structural model: Depressive symptom-domains							
NVS-E	Age, years	−0.03	0.001	−0.04	0.001	−0.01	0.002
	Sex, female	−0.02	0.02	0.004	0.02	−0.07	0.04
	Education level	0.02	0.01	0.01	0.01	0.01	0.01
	Married/cohabit	0.01	0.02	−0.02	0.02	0.02	0.03
	Live alone	0.02	0.02	0.02	0.02	0.04	0.04
	GAD-7	0.54***	0.003	0.47***	0.003	0.29***	0.005
	UCLA-3	0.29***	0.004	0.33***	0.003	0.15	0.007
	MoCA-5	−0.17***	0.002	−0.17***	0.002	−0.20	0.003
NVS-I	Age, years	−0.04	0.001	−0.01	0.001	−0.03	0.004
	Sex, female	−0.04	0.03	−0.01	0.02	−0.14*	0.08
	Education level	−0.07***	0.01	−0.10*	0.01	−0.11	0.03
	Married/cohabit	0.04	0.02	−0.01	0.02	0.13*	0.07
	Live alone	0.00	0.03	−0.02	0.02	0.01	0.07
	GAD-7	0.55***	0.003	0.45***	0.003	0.44***	0.007
	UCLA-3	0.11***	0.004	0.11***	0.003	0.27***	0.011
	MoCA-5	−0.04	0.003	0.02	0.001	−0.13	0.003
ARS	Age, years	−0.02	0.001	0.01	0.001	−0.07	0.004
	Sex, female	0.02	0.03	0.06	0.03	0.03	0.07
	Education level	−0.02	0.01	−0.01	0.01	−0.03	0.02
	Married/cohabit	−0.02	0.02	−0.08*	0.02	0.04	0.06
	Live alone	−0.003	0.02	−0.02	0.02	0.04	0.06
	GAD-7	0.48***	0.003	0.30***	0.004	0.11	0.006
	UCLA-3	0.07	0.004	0.09*	0.004	−0.21	0.011
	MoCA-5	−0.04	0.002	0.03	0.002	−0.08	0.004
CSS	Age, years	−0.08	0.001	−0.12*	0.001	−0.22	0.003
	Sex, female	−0.02	0.02	−0.03	0.03	−0.06	0.06
	Education level	−0.01	0.01	0.03	0.01	−0.09	0.02
	Married/cohabit	0.04	0.02	−0.02	0.02	0.02	0.05
	Live alone	0.06	0.02	0.12*	0.03	0.12	0.06
	GAD-7	0.63***	0.003	0.45***	0.003	0.60***	0.008
	UCLA-3	0.14***	0.004	0.31***	0.004	−0.08	0.009
	MoCA-5	−0.12***	0.002	−0.34***	0.002	−0.03	0.004

Table 3. Continued

Pathways	Model 1: Overall (N = 3,795)		Model 2: At-risk/mild (n = 3,146)		Model 3: Moderate and more severe (n = 649)	
	β	*SE*	β	*SE*	β	*SE*
χ^2/df	407.24/61 = 6.68		63.67/61 = 1.04			
p	<.001		.38			
SRMR	0.02		0.03			
RMSEA	0.04		0.01			
GFI	0.99		0.99			
CFI	0.97		0.99			
TLI	0.92		0.99			

Notes: ARS = arousal and regulatory systems; CFI = comparative fit index; CSS = cognitive and sensorimotor systems; *df* = degree of freedom; GAD-7 = Generalized Anxiety Disorder-7; GFI = goodness-of-fit index; MoCA-5 = Montreal Cognitive Assessment 5-Minute Protocol; NVS-E = negative valence systems and externalizing; NVS-I = negative valence systems and internalizing; PHQ-9 = Patient Health Questionnaire-9; RMSEA = root-mean-square error of approximation; SRMR = standardized root-mean-square residual; TLI = Tucker–Lewis index; UCLA-3 = UCLA 3-Item Loneliness Scale.
[a]The criteria for a good model fit are: $\chi^2/df \leq 5.0$, SRMR < 0.08, RMSEA < 0.08, GFI > 0.90, CFI > 0.90, TLI > 0.90.
$^*p < .05$. $^{**}p < .01$. $^{***}p < .001$.

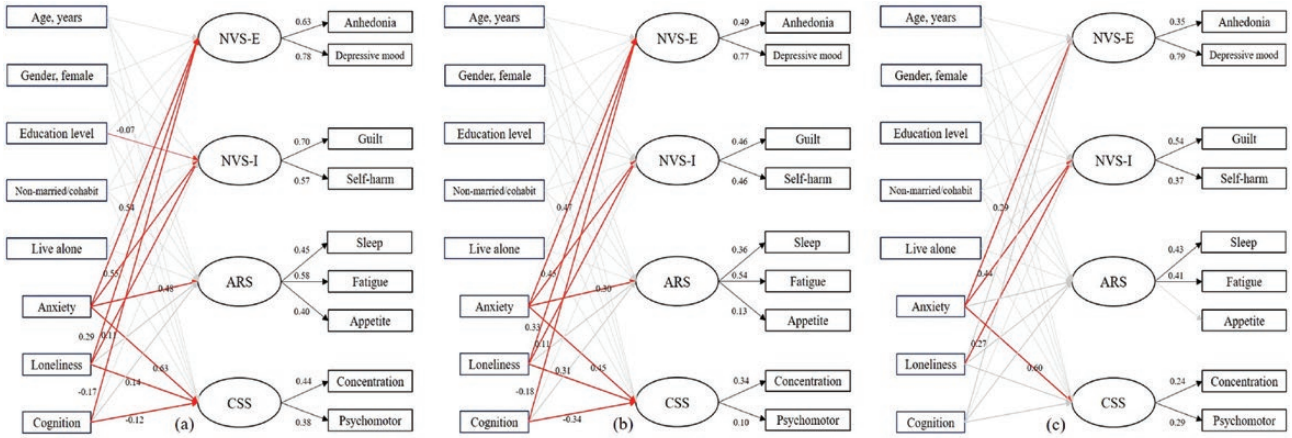

Figure 2. Multiple Indicator Multiple Causes (MIMIC) models for depression symptom-domains, anxiety, loneliness, cognition and demographics in (A) Model 1—overall sample (N = 3,795), (B) Model 2—at risk/mild (n = 3,146), and (C) Model 3—moderate and more severe depressive symptoms (n = 649). NVS-E = negative valence systems and externalizing; NVS-I = negative valence systems and internalizing; ARS = arousal and regulatory systems; CSS = cognitive and sensorimotor systems. Only standardized regression weights significant at the $p < .001$ level were reported, unstandardized regression weights and measurement errors were omitted for clarity.

depressive symptoms, including anhedonia, maintaining cognitive capacities, and improving insulin signaling (Toups et al., 2017). Cognition was not related to *ARS* or *NVS-I*, suggesting that global cognition may have little impact on somatic symptoms or how individuals relate to their emotional state.

Third, we also found that anxiety, loneliness, and cognitive functioning were differentially associated with depressive symptom-domains across different depression severity groups. The pattern observed in the at-risk/mild depressive symptom group was similar to that of the general population, and this is likely because the at-risk/mild symptom group formed 83% of the total sample, which also reflects a higher demand for selective prevention of late-life depression in the community. The complex associations between four depressive symptom-domains and other mental health conditions may contribute to misdiagnosis or ignorance of symptoms in the at-risk/mild depressive symptom group, suggesting the importance of screening for multiple mental health issues and more fine-grained examination. In the moderate and more severe depressive symptom (subclinical) group, anxiety was still significantly associated with *NVS-I* and *CSS*, loneliness was only associated with *NVS-I*, and cognition was no longer associated with any depressive symptom-domain. The fewer associations between depressive symptom-domains and loneliness and the absence of connections between depressive symptom-domains with cognition may imply the distinction of subclinical depression from other mental health conditions. Although literature suggested older adults may develop depressive symptoms in reaction to cognitive decline (Jajodia & Borders, 2011), we did not find any association between global cognition and depressive symptom-domains among those with subclinical depression, presumably, because this is a community sample without apparent cognitive impairment. More fine-grained assessments of cognition and multiple assessments over time are needed to unveil the complex relationship between cognition and depression. Nevertheless, the consistent association among anxiety, loneliness, and *NVS-I* across different severity groups may suggest the crucial roles

of anxiety and loneliness concerning how individuals evaluate themselves and their emotional state and risk for self-harm. This finding may also imply that to address the *NVS-I* domain of depression and to reduce self-harm risk, efforts can be made to increase individuals' social connectedness and reduce loneliness and anxiety.

Fourth, only a few demographic factors in this study were associated with different depressive symptom-domains; even for those with a significant association, the effect was small. Some of these findings are consistent with the literature; for example, education was negatively associated with depressive symptoms (Peyrot et al., 2015), and older age was not associated with a higher prevalence of depression in a Chinese community sample (Li et al., 2012). Other findings may fuel the discussions about the roles of certain demographic factors. Female sex was not associated with depressive symptom-domains other than in the subclinical population with *NVS-I* domain, which is inconsistent with the majority of the literature that women are at higher risk for depression (Maier et al., 2021). We speculate that for those at risk or with mild symptoms, the effect of sex became insignificant after multiple factors were considered. Marital status was not associated with any depressive symptom-domain, likely because of how we measured it, and some studies suggested that only "never being married" was associated with a higher incidence of depression (Conde-Sala et al., 2019). Lastly, although living alone is documented to be a risk factor for depression (Lim & Kua, 2011), in our sample, it was not associated with any of the depressive symptom-domains. Although living alone may predispose an individual to more loneliness and depression, older adults living alone in Hong Kong reported more social contact than their peers who lived with others, and the two groups showed similar levels of social and productive activities (Lou & Ng, 2012). Our sample was recruited from community centers, which provide space for social gatherings and regularly organize events for older adults, all adding to the protective factors of their mental health. Alternatively, it was also possible that for the "hidden older people," who are disengaged from the community and not recruited in this study, living alone may further elevates the risk of social isolation and in turn, be associated with poor mental health (Chau et al., 2014).

Limitations and Future Directions

Several limitations should be noted when interpreting the findings of this study. First, given its cross-sectional design, the study could not demonstrate variance in the impact of anxiety, loneliness, or cognition on depressive symptoms within an individual over time. Second, the PHQ-9 was used as a screening tool among community-dwelling older adults without a clinical diagnosis. Therefore, the current findings might not be generalizable to clinical populations of older adults. Third, the majority of the current sample was at risk or with mild depressive symptoms, which might influence the results of the MIMIC model in the overall population. Fourth, the current sample is community-dwelling older Chinese recruited through NGOs in Hong Kong, a more developed region than most of the cities in Mainland China, and boasts a mixture of traditional Han Chinese, ethnic Southeastern Chinese, and Western culture. Therefore, the findings from this sample may not be generated for the overall older Chinese, a much more diverse population with different subcultures and lifestyles. Fifth, this study only included a few risk factors, and some important factors, such as physical health, were not collected. Future investigations could consider multiple and repeated measures of depression, including more documented risk factors such as physical health condition and comparing the domains of depressive symptoms between the general older adult population and clinical samples.

Conclusion

To sum up, the findings of this study confirmed the utility of the RDoC framework in understanding depressive symptom-domains in community-dwelling older Chinese, and the differential associations between different depressive symptom-domains and anxiety, loneliness, and cognition may inform more personalized care. Individuals with anhedonia and depressive mood (*NVS-E*) may also exhibit anxiety symptoms, cognitive problems, and feelings of loneliness, especially among those at risk of or with mild depressive symptoms. Therefore, they are more likely to benefit from comprehensive preventive care, for example, group exercise and healthy lifestyle intervention. For individuals with feelings of inappropriate guilt and self-harm thoughts (*NVS-I*), anxiety symptoms and loneliness are likely to co-occur regardless of depressive symptom severity, which may infer higher resistance and relapse if the intervention targets depressive symptoms only. More indicated prevention and treatment addressing meaning in life, self-worthiness, and expanding social network are needed for those with *NVS-I* domain symptoms. Finally, for individuals who report more somatic or cognitive complaints (*ARS* and *CSS* domains), their depression may be masked or overlooked if no symptom is reported in the *NVS* domain; more fine-grained assessment is needed, and intervention for their mental well-being may consider their anxiety level as well.

Supplementary Material

Supplementary data are available at *Innovation in Aging* online.

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Conflict of Interest

None.

Data Availability

The data, analytical methods, and materials that support the findings of this study are available from the corresponding author upon reasonable request. The study reported in the manuscript was pre-registered with ClinicalTrials.gov (NCT03593889).

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