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Chronic Lung Diseases and Depressive Symptoms in Older Adults: Insights from Observational Studies and Mendelian Randomization

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Introduction: To elucidate the currently unknown relationship between chronic lung diseases (CLDs) and depressive symptoms among older adults.

Methods: A total of 8079 older adults from China Longitudinal Aging Social Survey (CLASS) and 1119 individuals from a Sichuan Province cohort were included in this study. We used regression analysis and propensity score matching (PSM) to assess the association between CLDs and depressive symptoms among older adults, while the causal relationship was assessed using Mendelian randomization (MR). Our sensitivity analyses included heterogeneity tests, tests of multiple validity, and leave-one-out tests. A two-way mediation analysis was also used to assess the mediating role of basic activities of daily living (BADL) between CLDs and depressive symptoms.

Results: In this cross-sectional study, we found that depressive symptoms significantly ($P < 0.001$) increased the risk of CLDs ($\beta = 0.047$). The robustness test showed that there were significant association between CLDs and depressive symptoms ($\beta = 0.220$, $P < 0.001$), Qi depression constitution ($\beta = 8.564$, $P < 0.001$). This finding was also confirmed through robustness tests using different PSM methods. The results of the inverse-variance weighting (IVW) analysis showed that depression increased the risk of idiopathic pulmonary fibrosis and asthma, with Beta coefficients of 2.822 [standard error (SE) = 1.087; $P = 0.009$] and −1.090 (SE = 0.491; $P = 0.027$), accordingly. The results of the IVW analysis showed that idiopathic pulmonary fibrosis and asthma increased the risk of depression, with Beta coefficients of 2.822 [standard error (SE) = 1.087; $P = 0.009$] and −1.559 (SE = 0.633; $P = 0.013$). The sensitivity analysis results confirmed the reliability of this conclusion. The mediating role of BADL was observed from depressive symptoms to CLDs.

Conclusion: Depressive symptoms are associated with an increased risk of CLDs, reduced BADL promote the risk of CLDs in older adults with depressive symptoms, but the underlying pathological mechanism still needs to be clarified in future research.

Keywords: cross-sectional study, propensity score matching, Mendelian randomization, chronic lung diseases, depressive symptoms

Introduction

Population aging has been a significant trend in the 21st century, and the size of China's older population exceeded 260 million in 2020.[1,2] In the context of a global aging population, mental health issues of older adults have gradually become the focus of attention for scholars at home and abroad. Depression has been one of the most common mental health problems in older adults, and the prevalence of depressive symptoms among them is 20.6%.[3] Depressive

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symptoms has been shown to be associated with a variety of worse outcomes, such as subjective cognitive decline, impaired activities of daily living, and increasing mortality.[4]

In recent years, chronic lung diseases (CLDs) affects approximately 454.6 million cases globally, which has become the fifth-largest cause of disability and third-largest cause of death throughout the world, threatening to the health of older adults.[5,6] CLDs shares characteristics such as chronic, progressive, lung function reduction, and inflammation, mainly including chronic obstructive pulmonary disease (COPD), chronic bronchitis, asthma, and idiopathic pulmonary fibrosis (IPF).[7] Previous studies have indicated an increased prevalence of depressive symptoms among individuals with specific kinds of CLDs, such as asthma and COPD.[8–10] Nevertheless, such cross-sectional studies have been conducted with samples of newly diagnosed or treated patients in hospitals, whose moods are more susceptible to being influenced by the progression of diseases, the side effects of treatment, and the hospital environment. The role of potential omitted variables, such as tobacco smoking in the relationship between CLDs and depressive symptoms warrants further consideration and exclusion.[11]

Basic activities of daily living (BADL) is defined as an important element for assessing physical activities and an individual's capacity to independently care for himself in managing daily tasks.[12] A few studies have demonstrated that there might be a relationship between depressive symptoms and BADL.[13] Specially, depressive symptoms frequently coexist with BADL disability. In addition, evidence suggested that BADL may influences the relationship between depressive symptoms and a series of sub-health conditions, such as sarcopenia, chronic diseases, and multimorbidity.[14–16] A cross-sectional study comprising over 4,000 older adults revealed a significant correlation between COPD and depressive symptoms.[17] Given these overlaps, we hypothesize that ADL may act as a mediator in the association between depressive symptoms and CLDs.

Therefore, this study aims to investigate the observational relationship between depressive symptoms and CLDs among older adults in China. The observational association was further extended to causal association using the Mendelian randomization (MR) method in order to rule out a series of omitted variables. Mediation analysis techniques were used to assess the mediation effect of BADL between CLDs and depressive symptoms.

Methods

Data Source and Sample

The nationally representative data for this study were obtained from China Longitudinal Aging Social Survey (CLASS) in 2014. The survey was jointly designed and executed by the Population and Development Research Center of Renmin University of China and the Institute of Gerontology. It is a national and continuous large-scale social survey project that targets Chinese citizens over the age of 60. The survey uses a stratified, multi-stage probability sampling method, and covers 28 provinces (autonomous regions, municipalities directly under the Central Government) in the Chinese mainland. We excluded participants who did not respond to the questions which we focused, 8079 older adults in this study left.

Furthermore, the random number table method was employed to select eight districts (counties) in Sichuan Province, with quota sampling conducted according to gender and regional population size. In accordance with the Kendall sample size estimation method, the number of instrumental variables under study was multiplied by a factor of between five and ten, and the invalid questionnaires were considered to expand the sample size by a further 20%. This resulted in an estimated sample size of 1,068, with 1,119 valid questionnaires ultimately included. Including criteria: (1) ≥60 years; (2) Be able to complete the survey; (3) Be resident in Sichuan Province; (4) Give informed consent and participate voluntarily in the study.

Assessment of Depressive Symptoms and Chronic Lung Diseases

In this study, CLDs was defined by whether a doctor has diagnosed it or not. Our definition of CLDs mainly includes respiratory diseases such as COPD, asthma, IPF, chronic bronchitis (excluding tumors or cancer).[18]

In CLASS-2014 database, we used the Center for Epidemiological Studies Depression Scale (CES-D-9) to evaluate the depressive symptoms of older adults. The scale consists of 9 items, of which three items evaluate positive emotions,

two items evaluate negative emotions, two items evaluate physical symptoms, and two items evaluate marginalization. Each item is scored using a three-level scoring system, with 0 point being counted as "little or no", 1 point counted as "some time", and 2 point counted as "most of the time". The total score of the scale is obtained by adding up the scores of each positive item through reverse coding, and the range of the total scale is 0–18 points; the higher the score, the more severe the depression symptoms of the subjects.[1,19] The Cronbach's α value of the scale was 0.750.

In CLASS-2014 database, we used basic activities of daily living (BADL) scale to evaluate BADL disability, which involved dressing, bathing or showering, eating, getting into or out of bed, using the toilet, and controlling urination and defecation.[20] The Cronbach's α value of the scale was 0.791.

In order to ascertain the robustness of the relationship between depressive symptoms and CLDs, we replaced the CES-D-9 with two alternative measures of depressive symptoms in a cohort of older adults in Sichuan Province. Firstly, depressive symptoms were assessed in older adults using a single item from the Chinese medicine quality of life-11 dimensions (CQ-11D) Scale.[21] The question posed was as follows: Are you currently experiencing feelings of anxiety, worry, nervousness, discouragement, or a lack of interest in engaging in activities, or are you feeling depressed, as indicated by a lack of positive affect, an inability to experience joy, or a lack of motivation?. The responses were categorized into four levels: "very good", "fairly good", "fairly poor" and "very poor". Furthermore, depressive symptoms in older adults were assessed using the "Qi depression constitution" dimension of the short version of the 30 items of TCM body Quality Table.[22] Prior research has indicated that the Qi depression constitution was strongly correlated with the presence of depressive symptoms.[23,24] The dimension comprises four entries, each representing a level of severity on a 5-point scale (1 = not at all, 5 = always).

Potential Covariates

Based on previous studies, we collected several potential confounding variables in this study. These variables included age, sex, education level, residence, and marital status.

Mendelian Randomization Study Design

This study assessed the causality and directionality of relationships between COPD, asthma, IPF, chronic bronchitis, and depression through an MR approach. MR approach is considered as a method identifying the causal relationship between the exposure and the outcome by using genetic variants for exposure as instrument variables (IV), which could utilize the dataset from large-sample genome-wide association studies (GWAS) for both "exposures" (as a risk factor) and "outcomes" (as a disease) and compensate typical shortcomings of observational studies. The three key assumptions of MR are as follows: ①Relevance assumption: Genetic variation (refers to IV) must be significantly associated with the exposure; ②Independence assumption: The IV must be independent of confounders between the exposure and outcome; ③Exclusion restriction assumption: The IV must influence the outcome solely through the exposure, with no alternative pathways. Genetic association data for the MR analysis were obtained from the publicly available IEU OpenGWAS project database (https://gwas.mrcieu.ac.uk/), which includes data from the UK Biobank. Specifically, the datasets comprised genetic data for COPD (ID: ukb-b-13447), asthma (ID: ukb-b-17219), IPF (ID: ebi-a-GCST90018120), chronic bronchitis (ID: ebi-a-GCST90038617), and depression (ID: finngen_R12_F5_DEPRESSIO). Sample sizes ranged from 198,000 to 484,000 individuals, and the number of single nucleotide polymorphisms (SNPs) ranged from 9.58 million to 16.38 million. This large scale ensures sufficient strength and quantity of IVs to meet MR study requirements.

To ensure reliability, SNPs significantly associated with the exposures ($P < 5\times10^{-8}$) were selected. Linkage disequilibrium (LD) pruning ($R^2 < 0.001$) was applied to reduce correlation among SNPs, minimizing bias caused by weak IVs. The primary analysis was conducted using the inverse variance weighted (IVW) method, which assumes all IVs are valid and free from horizontal pleiotropy. Sensitivity analyses were performed using MR-Egger, weighted median, and weighted mode methods to assess robustness and potential pleiotropy. Heterogeneity among IVs was evaluated using Cochran's Q statistic, while the MR-Egger intercept test was employed to detect horizontal pleiotropy. The strength of IVs was assessed by calculating the F-statistic, with an $F > 10$ considered sufficient to avoid weak

instrument bias. Additionally, leave-one-out analysis was conducted to ensure that results were not driven by any single SNP. These analyses ensured that the instrumental variables selected were both robust and valid for causal inference.

Specific information is provided in the Supplementary Table S1. All analytical data were derived from publicly available databases, and no additional informed consent was required.

Statistical Analysis

The data were processed and analyzed using R 4.3.2, Stata 16.0, and AMOS 26.0. Firstly, descriptive statistical analysis was performed on the research data to compare the differences in scores of various variables among older adults with different demographic characteristics. Secondly, multiple linear regression was used to analyze the correlation between CLDs and depressive symptoms based on CLASS-2014. Then, we utilized propensity score matching (PSM) to identify covariates and perform propensity score analysis. Three PSM methods—including one-to-one matching, radius matching, kernel matching—were adopted in this study. Two multiple linear regressions were established to analyze the correlation between Qi depression constitution, anxiety/depression and CLDs for the robustness test based on the external cohort. Mediating analysis was performed to explore the pathway linking depressive symptoms and CLDs based on CLASS-2014. All statistical tests in this study were performed at a significance level of $P < 0.05$ via a two-tailed approach.

Results

Baseline Characteristics

A total of 8079 individuals participated in the baseline survey of CLASS in 2014 (Table 1). The study population was divided into two groups: the non-CLDs group with 7564 participants and the CLDs group with 515 participants. All covariates in Table 1 were statistically imbalanced ($P < 0.001$). In addition, a total of 1119 individuals participated in the baseline survey from Sichuan cohort, which was divided into two groups (Supplementary Table S2).

Table 1 Characteristics of the Participants Attending the Baseline Survey of CLASS in 2014

Variable	N (%)	Mean±SD	t/F	*P*
Gender			−4.919	<0.001
Male	4380 (54.21%)	4.368+3.475		
Female	3699 (45.79%)	4.759+3.654		
Age			11.361	<0.001
60–69 years old	4740 (58.67%)	4.398+3.544		
70–79 years old	2465 (30.51%)	4.702+3.587		
80 years old and above	874 (10.82%)	4.922+3.561		
Education level			83.809	<0.001
Illiterate	1589 (19.67%)	5.703+3.812		
Private schooling or literacy class	208 (2.57%)	5.399+3.68		
Primary school	2716 (33.62%)	4.844+3.547		
Junior high school	1917 (23.73%)	3.979+3.326		
Senior high school or vocational school	1036 (12.82%)	3.705+3.182		
Junior college and above	613 (7.59%)	3.152+3.084		
Residence			−15.615	<0.001
Urban	5310 (65.73%)	4.107+3.369		
Rural	2769 (34.27%)	5.392+3.769		
Marital status			15.306	<0.001
Have no partner	2308 (28.57%)	5.494+3.842		
Have a partner	5771 (71.43%)	4.169+3.373		
Chronic lung diseases			−10.199	<0.001
No	7564 (93.63%)	4.443+3.505		
Yes	515 (6.37%)	6.087+4.037		

Patients with CLDs Had Increased Risk of Depressive Symptoms

To assess the association between CLDs and depressive symptoms, a multiple linear regression model was constructed based on CLASS-2014 (Table 2). Participants with CLDs had increased odds of depressive symptoms when compared with participants without CLDs ($B = 0.688$, $P < 0.001$). In light of the potential for confounding factors to influence the regression results, this study employed PSM as a means of correcting for such effects. The samples were divided into two groups, one comprising individuals with CLDs and the other comprising individuals without CLDs. The experimental and control groups were then matched using three matching methods: 1:1 nearest-neighbour matching, 1:4 nearest-neighbour matching, and kernel matching. The results demonstrated that the two groups of samples after matching exhibited a high degree of balance, with the majority of observations falling within the range of common values. Additionally, the kernel density curves of the two groups of samples after matching exhibited a strong fit, aligning with the assumption of commonality. The standardized deviation of the treatment groups was less than 10% in the matched samples, indicating an improved overall matching effect (Supplementary Figure S1). This is further supported by Supplementary Table S3. The average treatment effect (ATT) values of all models are less than zero and statistically significant ($P < 0.001$), indicating that there is a significant role and effect of CLDs prevalence on depressive symptoms in older adults.

To ascertain the veracity of the assertion that there is a robust relationship between CLDs and depression, replicated experiments were conducted on a cohort of older adults in Sichuan Province. Participants with CLDs had increased odds of depression when compared with participants without CLDs (Model 2: $B = 8.564$, $P < 0.001$; Model 4: $B = 0.220$, $P < 0.001$, Table 3). The results of different models remained consistent, with Model 2 indicating that CLDs were associated with Qi depression constitution in older adults, and Model 4 suggesting that CLDs were associated with the presence of anxiety-depressive symptoms in older adults. In light of the aforementioned evidence, it can be concluded with a high degree of confidence that there is a robust association between CLDs and depressive symptoms in older adults.

Table 2 The Association Between CLDs and Depression of CLASS in 2014

	B	SE	β	t	P
Constant	10.601	0.335		31.651	<0.001
Gender	−0.095	0.076	−0.013	−1.257	0.209
Age	−0.102	0.056	−0.020	−1.833	0.067
Marital status	−1.027	0.086	−0.130	−11.890	<0.001
Education level	−0.305	0.027	−0.126	−11.257	<0.001
Residence	0.602	0.082	0.080	7.387	<0.001
Chronic lung diseases	0.688	0.147	0.047	4.668	<0.001

Note: R^2=0.200, Adjusted R^2=0.199, F=288.272, P<0.001.

Table 3 The Association Between CLDs and Depression of Sichuan Cohort

Variable	Dependent Variable:Qi Depression Constitution						Dependent Variable:Anxiety/Depression					
	Model 1			Model 2			Model 3			Model 4		
	β	*SE*	t	*β*	*SE*	t	*β*	*SE*	t	*β*	*SE*	t
Gender	5.371	1.236	4.346***	5.556	1.217	4.565***	0.099	0.038	2.618**	0.104	0.038	2.771**
Age	−0.718	0.903	−0.795	−1.177	0.892	−1.319	−0.054	0.028	−1.929	−0.065	0.028	−2.369*
Residence	0.774	1.201	0.644	0.547	1.183	0.463	−0.010	0.037	−0.270	−0.016	0.037	−0.432
Marital status	−4.243	1.494	−2.840	−4.600	1.472	−3.125	0.005	0.046	0.115	−0.004	0.045	−0.085

(*Continued*)

Table 3 (Continued).

Variable	Dependent Variable:Qi Depression Constitution						Dependent Variable:Anxiety/Depression					
	Model 1			Model 2			Model 3			Model 4		
	β	*SE*	t	*β*	*SE*	t	*β*	*SE*	t	*β*	*SE*	t
Education level	0.262	0.404	0.649	0.264	0.397	0.664	0.026	0.012	2.058*	0.026	0.012	2.084*
Chronic lung diseases				8.564	1.417	6.045***				0.220	0.044	5.014***
R	0.159			0.237			0.121			0.191		
R^2	0.025			0.056			0.015			0.036		
F	4.803			36.544			2.735			25.144		

Notes: ***P<0.001, **P<0.01, *P<0.05. Model 1: Crude model. Model 2: Adjusted for age+gender+residence+marital status+education level; Model 3: Crude model. Model 4: Adjusted for age+gender+residence+marital status+education level.

There Were Bidirectional Causal Relationship Between IPF, Asthma and Depression

To investigate the casual linkage of depressive symptoms on CLDs, four diseases including COPD, asthma, IPF, and chronic bronchitis were used as exposures. Depression data from the database served as the outcome variable. For these IVW assessments (Table 4), genetically predicted depression was both associated with IPF and asthma, with Beta coefficients of 2.822 [standard error (SE) = 1.087; P = 0.009] and −1.090 (SE = 0.491; P = 0.027), accordingly. All sensitivity analyses produced generally consistent results. The MR estimates were neither heterogeneous nor horizontally multidimensional, indicating that the causal effect estimates were reliable. No causal relationship was found between depression and COPD, chronic bronchitis (Supplementary Figure S2).

To investigate the casual linkage of CLDs on depression, depression was used as exposures. Four CLDs data from the database served as the outcome variables. For these IVW assessments (Table 4), genetically predicted IPF and asthma were both associated with depression, with Beta coefficients of 2.822 [standard error (SE) = 1.087; P=0.009] and −1.559 (SE = 0.633; P = 0.013), accordingly. All sensitivity analyses produced generally consistent results. The MR estimates were neither heterogeneous nor horizontally multidimensional, indicating that the causal effect estimates were reliable. No causal relationship was found between COPD, chronic bronchitis and depression (Supplementary Figure S3).

Reduced BADL Promote the Risk of CLDs in Older Adults with Depressive Symptoms

Table 4 displayed the mediating effect of BADL on the relationship between depressive symptoms and CLDs, as determined using the binary regression analysis and linear regression analysis. In three models in Table 5, depressive symptoms were associated with an increased likelihood of developing CLDs (OR = 1.057, 95% CI = 1.030–1.085, P < 0.001) and decreasing BADL (OR = −0.025, P < 0.001), BADL also demonstrated a notable positive correlation with the incidence of CLDs (OR = 1.120, 95% CI = 1.003–1.250, P < 0.05). The 95% CI obtained by the

Table 4 Associations Between Depression and Chronic Lung Diseases Using Mendelian Randomization

Exposures	Outcomes	IVW		MR Egger		Weighted Median		Weighted Mode		Simple Mode	
		Beta (SE)	*P*	Beta (SE)	*P*	Beta (SE)	*P*	Beta (SE)	*P*	Beta (SE)	*P*
IPF	Depression	2.822 (1.087)	0.009	1.697 (1.409)	0.235	1.528 (1.583)	0.334	1.317 (1.449)	0.368	1.317 (1.449)	0.368
Asthma	Depression	−1.559 (0.633)	0.013	−1.370 (2.263)	0.552	−1.358 (0.650)	0.037	−1.594 (0.860)	0.079	−1.052 (1.122)	0.359
Depression	IPF	2.822 (1.087)	0.009	1.697 (1.409)	0.235	1.528 (1.495)	0.307	1.317 (1.309)	0.349	3.197 (3.946)	0.422
Depression	Asthma	−1.090 (0.491)	0.027	−1.415 (1.446)	0.332	−1.003 (0.517)	0.052	−1.127 (0.834)	0.182	−0.569 (1.135)	0.618

Abbreviations: IPF, Idiopathic pulmonary fibrosis; IVW, inverse-variance weighted; MR, Mendelian randomization.

Table 5 Regression Analysis of the Mediating Effect of Basic Activities of Daily Living

Variable	Model 1		Model 2		Model 3	
	OR	95% CI	*β*	*t*	OR	95% CI
Gender (male)			0.033	1.760		
Female	0.632***	0.515–0.775			0.629***	0.513–0.772
Age (60–69 years old)			−0.143	−10.440***		
70–79 years old	1.525***	1.241–1.874			1.543***	1.255–1.896
80 years old and above	1.559**	1.152–2.110			1.641**	1.209–2.228
Educational level(illiterate)			−0.004	−0.548		
Private schooling or literacy class	1.049	0.622–1.769			1.042	0.617–1.759
Primary school	0.779	0.601–1.009			0.781	0.603–1.013
Junior high school	1.049	0.785–1.403			1.054	0.788–1.410
Senior high school or vocational school	0.883	0.617–1.264			0.888	0.620–1.271
Junior college and above	0.728	0.456–1.161			0.739	0.463–1.180
Residence (urban)			0.064	3.193**		
Rural	1.256*	1.021–1.546			1.241*	1.008–1.528
Marital status (not married)			−0.014	−0.635		
Married	0.911	0.733–1.132			0.916	0.737–1.139
Self assessed health status (Very unhealthy)			0.107	12.060***		
Relatively unhealthy	0.641**	0.465–0.883			0.602**	0.435–0.832
Commonly	0.379***	0.272–0.530			0.349***	0.249–0.491
Relatively healthy	0.248***	0.173–0.354			0.228***	0.159–0.328
Very healthy	0.147***	0.089–0.243			0.136***	0.082–0.225
Depressive symptoms	1.057***	1.030–1.085	−0.025	−9.071***	1.061***	1.033–1.089
BADL					1.120*	1.003–1.250
Constant	0.144		17.744		0.020	

Notes: *P<0.05.**P<0.01.***P<0.001. Model 1: Binary regression analysis of depressive symptoms and chronic lung diseases; Model 2: Linear regression analysis of depressive symptoms and basic activities of daily living; Model 3: Binary regression analysis of basic activities of daily living and chronic lung diseases.

RMediation package of R software using the product distribution method of testing was found to be equal to −5.786e-03 and −7.977e-05, respectively. Notably, these values did not contain zeros and indicated a significant mediating effect,[25] which means that BADL plays a mediating role from depressive symptoms to CLDs. Additionally, we did not observe a possible mediating role of BADL from CLDs to depressive symptoms (Supplementary Tables S4 and S5).

Discussion

In this study, we investigated the correlation between CLDs and depressive symptoms in older adults using data from CLASS database and a cohort from Sichuan Province. Our study suggests that there was a noticeable correlation between CLDs and depressive symptoms, which align with previous studies.[26] The external cohort was used to validate the relationship between Qi depression constitution, anxiety/depressive symptoms and CLDs, which indicated the relationship between CLDs and depressive symptoms was well-established and robust.

Additionally, we applied the MR method to evaluate the causal effect of depression on CLDs, in order to rule out potential relationships where confounders such as smoking play a role in this relationship.[11] In order to gain insight into CLDs, COPD, asthma, IPF, and chronic bronchitis were selected for observation. The investigation yielded evidence to suggest a bidirectional causal relationship between asthma and depression. Similarly, a study based on NHANES and MR also demonstrated a significant correlation and potential causal relationship between asthma and depression.[27] Prior research has demonstrated that depression is a prevalent comorbidity of IPF.[28] In this study, we demonstrated for the first time a bidirectional causal relationship between IPF and depression. While this study did not identify a causal relationship between COPD and depression, this finding differs from previous literature.[11,29] This discrepancy may be attributed

to the diverse population sources utilized in the data selection process. Furthermore, there is no causal relationship between chronic bronchitis and depression. In conclusion, it can be posited that there is a causal relationship between CLDs and depression at the genetic level. However, results reported in Zheng et al's study demonstrate a bidirectional causal relationship between CLDs and depressive symptoms based on epidemiological data.[30] Further longitudinal and meta-analysis studies are still needed to verify the causal relationship between more kinds of CLDs and depression in older adults.

Interestingly, this results obtained from the CLASS database revealed that BADL acted as a mediator from depressive symptoms to CLDs, which indicated that the prediction ability of depressive symptoms on CLDs among them was not entirely and directly related to CLDs, but rather that depressive symptoms predicts CLDs through partial mediation of BADL. According to the research from Chou et al, depressive symptoms may have an impact on physical disability.[31] A longitudinal also reported that depressive symptoms increases the risk of subsequent ADL disability by 67%.[32] A lack of physical activity, which is a common consequence of chronic depressive symptoms, has been linked to increased levels of systemic inflammation.[33] This, in turn, has been identified as a contributing factor to an increased susceptibility to CLDs.[15,30] Emerging evidence has also suggested biological pathways exist between depression and CLDs development. Depression is associated with activation of the hypothal-amic-pituitary-adrenal axis and increased proinflammatory cytokines, which promote systemic and airway inflammation and pulmonary infection, finally leading to impairment of lung tissue and function as represented by reduced airflow and chronic cough.[33–36] However, BADL did not appear to play the same mediating role from CLDs to depressive symptoms.

There are still some limitations in this study. First, CLDs and depression were defined on the basis of the questionnaire from the CLASS database, which may be influenced by social factors, inevitably producing measurement bias. Second, while we try to control over confounding factors in transethnic MR research, some potential factors and comorbidities cannot be entirely ruled out. Third, this study did not explore the relationship between the severity of CLDs (eg, symptomatology, degree of pulmonary decompensation) and the degree of depressive symptoms. Further exploration of this relationship is necessary and should be a priority in future studies. Finally, we only selected several representative diseases for MR study. In future research, a more extensive range of diseases should be considered to investigate the casual association between CLDs and depression.

Conclusions

There is a correlation between CLDs and depressive symptoms in older adults from China, and BADL plays a mediating role from depressive symptoms to CLDs among older individuals. There were also bidirectional causal relationships between asthma, IPF and depression. Therefore, relevant agencies should continue to pay attention to the depression status of older people, especially those with CLDs. Due to group differences in depression among older adults, interventions should be implemented for different demographic characteristics and types of groups that allow them to fully exercise their BADL. This is important for changing the mental health of older persons, improving their quality of life, reducing the economic burden of disease on families and society, and realizing healthy ageing.

Abbreviations

CLASS, Chinese Longitudinal Aging Social Survey; CLDs, Chronic Lung Diseases; BADL, Basic Activities of Daily Living; MR, Mendelian Randomization.

Data Sharing Statement

The data used in this study are available upon reasonable request from the Institute of Gerontology and the National Survey Research Center at Renmin University of China. The dataset can be accessed via the following link: http://class.ruc.edu.cn/index.php?r=index/index&hl=en. Yisong Yao obtained permission to access and utilize all relevant data for this study.

Ethics Approval and Consent to Participate

Mendelian randomization analysis was conducted using publicly available data resources (eg, UK Biobank and IEU OpenGWAS project). All datasets had received prior ethical approval and were shared under open-access terms. This study did not involve direct contact with participants or their personal information, thereby exempting it from further ethical review. All procedures performed in the study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 helsinki declaration and its later amendments or comparable ethical standards. The survey was also conducted within the article 38, 39, and 40 of the Constitution of People's Republic of China and the legal framework governed by Chapter I, Article 9 from the statistics law of the People's Republic of China. Therefore, the study was not reviewed by ethics committee. Verbal informed consent was obtained from all individual participants included in the study. Verbal informed consent was acceptable and was not reviewed by ethics committee. Moreover, the interviewer also had documented the more details information on the process of obtaining informed consent, which included whether agree to attend this study, the time of agree to attend this study, the reasons of disagree to attend this study, and so on. Details of informed consent was stored by the Institute of Gerontology and National Survey Research Center at Renmin University of China. Our study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Yantai Yuhuangding Hospital (NO.2025-161).

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in this work.

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