

The Role of Chronic Disease Numbers in the Relationship Between Living Alone and Depression: A Four-Way Decomposition Analysis in a Cross-Sectional Study of Older Adults

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Objective: Living alone is becoming increasingly common among the elderly population, and there is a close relationship between living alone and chronic diseases in relation to depression. However, the interplay between them has not been fully investigated. This study aims to explore the role of the number of chronic diseases in the relationship between living alone and depressive symptoms among older adults in China.

Patients and methods: A population-based cross-sectional study was conducted in Guangxi, China, involving 10,370 older adults (aged ≥ 65 years) living in the community. Using the four-way decomposition analysis, we evaluated: (1) The direct impact of living alone on depression; (2) The mediating role of the number of chronic diseases when controlling for potential confounding factors.

Results: The risk of depressive symptoms in older adults living alone was significantly higher than that in older adults cohabiting (adjusted OR = 1.66, 95% CI: 1.57, 1.76). Mediation analysis showed that 71.64% of the total effect was a controllable direct effect (CDE: $\beta = 0.384$, 95% CI: 0.058, 0.709), and 11.91% of the total effect was mediated by the number of chronic diseases (pure indirect effect: $\beta = 0.046$, 95% CI: 0.005, 0.086). The effects of reference interaction (INTref) and mediating interaction (INTmed) did not reach statistical significance.

Conclusion: The number of chronic diseases plays a partial mediating role between living alone and depression. Although chronic diseases do mediate the relationship between living alone and depression to some extent, the majority of the effect is directly attributable to the state of living alone. These findings highlight the significant impact of living alone on depression in older adults and suggest that mental health interventions targeting older adults living alone should focus on enhancing social support and emotional care to effectively reduce the risk of depression.

Keywords: living alone, depressive symptoms, chronic disease, older adults, four-way decomposition

Introduction

As the global aging process accelerates, China's population is aging faster than most high-income countries.¹ By 2020, the proportion of the population aged 65 and over in China has reached 13.5%,² and is expected to reach 26.1% by 2050,³ which means that China is facing serious aging challenges.⁴ The proportion of older adults living alone in China is currently at 12.5%,⁵ higher than the global average of 12% of the population aged 60 and over living alone.⁶ The increase in older adults living alone is attributed to factors such as increased population mobility,⁷ extended life expectancy,⁸ and higher pension levels.⁹

Older adults who live alone without spouses, children, or family members, face multiple health risks.^{10,11} They have higher rates of chronic disease than those living with family members¹² and experience significant depressive symptoms

due to social isolation and loneliness.¹³ Although a large number of studies have explored the association between living alone and depressive symptoms,^{14–16} conclusions have been inconsistent. A meta-analysis showed that people living alone had a significantly higher risk of depressive symptoms than those with other living arrangements,¹⁷ indicating the potential harm to mental health of living alone.

Living alone impacts the health of older adults, increasing the risk of cardiovascular disease, stroke, and diabetes.^{18–21} Older adults with conditions such as dementia often struggle to adequately treat their depressive symptoms.^{22,23} Living alone with multiple health issues is a major challenge in managing older adults' health and a useful indicator for assessing depression risk, guiding preventive strategies.²⁴

The relationship between chronic diseases and depressive symptoms has garnered significant attention. The prevalence of chronic diseases is positively correlated with the severity of depressive symptoms in older adults, with higher numbers of chronic diseases associated with more severe symptoms.^{25–27} Depression and chronic diseases have a bidirectional relationship,²⁸ and the World Health Organization (WHO) Global Burden of Disease study indicates that individuals with chronic diseases are more likely to experience depression. Moreover, people with multiple chronic diseases are two to three times more likely to develop depression than those without chronic or multiple diseases.²⁵ Therefore, chronic diseases not only threaten physical health, but also increase the risk of depressive symptoms.²⁹

Although previous studies have explored the associations between living alone, chronic illness, and depressive symptoms, the impact of chronic illness on the relationship between living alone and depressive symptoms remains unclear and has not been fully investigated. Most existing studies focus solely on direct associations, overlooking the complex interactions between chronic illness and mental health outcomes. This study, based on the biopsychosocial model, examines the relationship between the number of chronic illnesses, living alone, and depressive symptoms in older adults. By using a four-way decomposition method, we can simultaneously consider the direct effects, indirect effects, and interactions between these factors. This approach offers a more comprehensive understanding of how living alone affects mental health. Specifically, the four-way decomposition method helps us understand what proportion of the total effect can be attributed to the complex relationship between chronic illness, living alone, and depressive symptoms, including direct effects, indirect effects, and their interactions. This method is particularly suitable for situations where multiple variables interact and provides strong evidence for related interventions.

Methods

Subjects

In 2023, 35 community and village health facilities spread throughout 14 cities in Guangxi, China, recruited older adults for this cross-sectional study. Their primary caregivers gave some objective information, and health examinations and questionnaires were administered. The two requirements for inclusion were satisfied: (1) being 65 years of age or older, and (2) being a resident of the communities that were sampled. Exclusion criteria include: (1) not finishing all the surveys and dropping out, and (2) having a major cognitive disability, mental disease, or other health condition that could affect the survey's results, such as an inability to comprehend or respond to the questionnaire. Health professionals with consistent training evaluated and gathered all of the data. An electronic questionnaire method was used to enter all of the data into a database. Three subject categories with incomplete data were eliminated throughout the data cleaning process: living arrangements, status of chronic diseases, and depressed symptoms. In the end, 11,370 participants were included in the analysis. All participants gave their informed consent, and the study was authorized by the Guangxi Medical University Second Hospital Research Ethics Committee (No. 2023-KY0905).

Measurement

Exposure Variable

Participants were classified as living alone if they had resided without any core family members (spouse, parents, children, or siblings) for ≥ 11 months in the past year. When assessing living-alone status, we also asked participants whether they had family members living nearby who provided daily support. Even if participants received daily support

from family members (such as occasional visits or help with errands), they were still considered as “living alone” as long as they had not lived with core family members during the past year.

Outcome

The Patient Health Questionnaire - 9 (PHQ - 9) is a validated 9-item self-reporting tool. This scale assesses depressive symptoms in the previous two weeks. The score for each item ranges from 0 (“None at all”) to 3 (“almost every day”), with a total score ranging from 0 to 27. A score of ≥ 5 indicates depressive symptoms.³⁰

Mediator

Participants self-reported their chronic disease status by responding to the question: “Has a doctor or other healthcare professional ever diagnosed you with any of the following chronic conditions?” Each reported condition was coded as “1”, with a “0” assigned otherwise. The chronic disease score was calculated as the sum of all reported conditions. The disease list comprised 20 prevalent chronic conditions selected based on ICD-10 classification and prior epidemiological studies:³¹ hypertension, coronary heart disease, diabetes mellitus, cerebrovascular disease, chronic bronchitis, cancer, renal disease, liver disease, gastrointestinal disorders, tuberculosis, rheumatoid arthritis, cervical/lumbar spine disorders, reproductive disorders, prostate disorders, urologic disorders, glaucoma/cataracts, osteoporosis, mood disorders, mental disorders, and neurological disorders. A participant was classified as having a chronic condition if they reported at least one physician-diagnosed illness from this list.

Covariates

The covariates in this study include age, residence (city, rural), gender (male, female), poor (no, yes), marital status (no married, married), educational period (0, 1–6, ≥ 7).

Statistical Analyses

SPSS 25.0 and Stata 18.0 were used for the analysis. Measurement data were expressed as mean and standard deviation, whereas count data were expressed as frequency and percentage. In this study, we used the four-way decomposition method (implemented through the med4way package in Stata³²) to analyze the association between living alone and depression, as well as to investigate the interactions or mediating effects with the number of chronic diseases, including both the overall and direct effects of these effects. The four-way decomposition approach is an analytic framework for integrating interaction and mediation effects by breaking the total effect down into four components: an effect that is neither mediated nor interacted, a pure interaction effect, an effect that is both mediated and interacted, and a pure mediation effect. This decomposition reveals the following shares of the total effect: purely indirect effects (mediated effects, PIE), interactions between exposure and mediator (referential interactions, INTref), joint effects of the two (mediated interactions, INTmed), and direct effects that are neither mediated nor interacted (controlled direct effects, CDE). This decomposition is crucial for understanding the specific contributions of both interaction and mediating mechanisms to the observed outcomes. We controlled for several confounding variables, including age, residence, gender, marital status, and educational period. Bias-corrected 95% confidence intervals were calculated using 1000 bootstrap resampling iterations. Intervals that do not include zero indicate statistically significant effects. [Figure 1](#) shows the exact path of the four-way decomposition.

Results

Sample Characteristics

[Table 1](#) shows the individuals’ characteristics based on their depressive symptoms. In a sample of 10,370 people, 44.3% were men and 55.7% were women, with an age range of 65–101 years and a mean age of 72 (68, 77) years. 89.6% of older adults cohabitated, while 10.4% lived alone. 32.5% (3372) of older adults had no chronic diseases, 37.5% (3888) had one, and 30.0% (3110) had two or more. 7.2% of individuals reported experiencing depressed symptoms. Univariate analyses revealed a strong association between depression and sociodemographic characteristics (age, gender, residence, education, marital status, and living arrangements) and chronic diseases (all $p < 0.0001$). Older adults living alone had considerably greater rates of depressive symptoms compared to those living jointly (11.3% vs 6.7%, $p < 0.001$). The

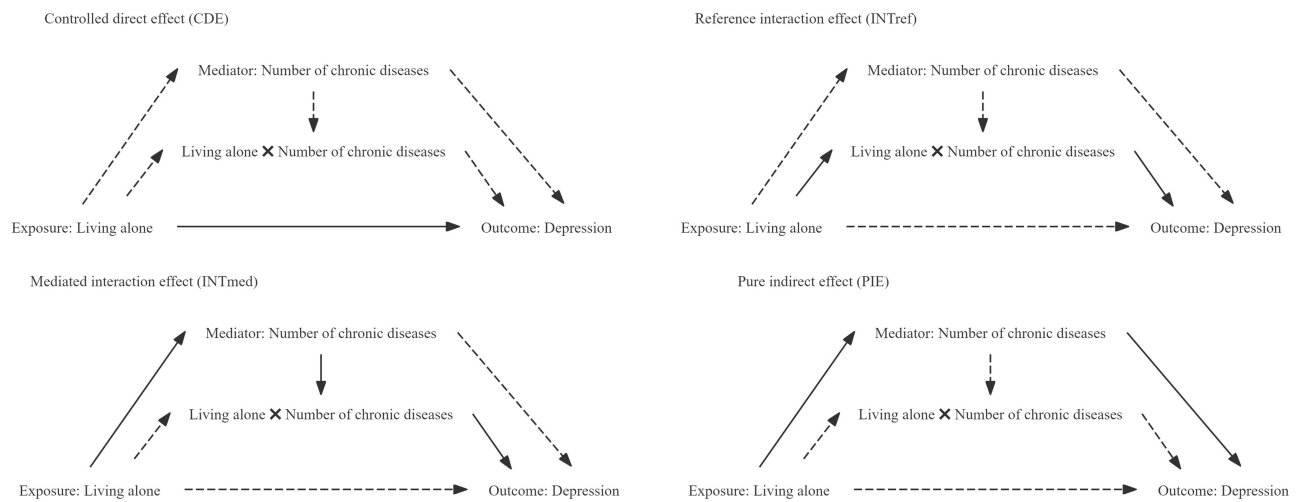


Figure 1 A conceptual framework for four-way decomposition mediation analysis.
Notes: Solid lines indicate actual paths, while dashed lines indicate blocked paths.

number of chronic diseases is closely related to the occurrence of depressive symptoms. The incidence of depressive symptoms is significantly higher among people with more chronic diseases.

Of the 20 chronic conditions assessed, hypertension was most prevalent (33.0%), followed by cervical/lumbar spondylosis (13.7%) and rheumatoid arthritis/joint disease (9.4%); all other conditions had prevalence rates below 8% (Table 2).

Table 3 shows the results of binary logistic regression analysis. Taking depressive symptoms (encoded as 0 = non-existence, 1 = existence) as the dependent variable and after adjusting for potential confounding factors (age, gender,

Table 1 Basic Characteristics of Participants and One-Factor Analysis

Variables	Total [n (%)]	Depressive Symptom [n (%)]		P
		Normal	Depression	
Age		72 (68, 77)	74 (69, 80)	<0.001
Residence				<0.001
City	5337 (51.5%)	5004 (93.8%)	333 (6.2%)	
Rural	5033 (48.5%)	4624 (91.9%)	409 (8.1%)	
Gender				<0.001
Male	4590 (44.3%)	4346 (94.7%)	244 (5.3%)	
Female	5780 (55.7%)	5282 (91.4%)	498 (8.6%)	
Poor				0.316
No	8824 (85.1%)	8202 (93.0%)	622 (7.0%)	
Yes	1546 (14.9)	1426 (92.2%)	120 (7.8%)	
Marital status				<0.001
No married	3132 (30.2)	2826 (90.2%)	306 (9.8%)	
Married	7238 (69.8%)	6802 (94.0%)	436 (6.0%)	
Living arrangements				<0.001
Cohabitation	9287 (89.6%)	8667 (93.3%)	620 (6.7%)	
Living alone	1083 (10.4%)	961 (88.7%)	122 (11.3%)	
Educational period				<0.001
0	1831 (17.7%)	1616 (88.3%)	215 (11.7%)	
1–6	5117 (49.3%)	4751 (92.8%)	366 (7.2%)	
≥7	3422 (33.0%)	3261 (95.3%)	161 (4.7%)	
Chronic disease number		1 (0.00, 2.00)	2 (1.00, 3.00)	<0.001

Table 2 The Prevalence of 20 Chronic Diseases Among the Older Adults

Sort	Chronic Disease	Number	Proportion (%)
1	Hypertension	3885	33.00%
2	Cervical/lumbar spondylosis	1613	13.70%
3	Rheumatoid/arthritis	1107	9.40%
4	Diabetes	878	7.50%
5	Gastroenteritis	759	6.50%
6	Heart disease	667	5.70%
7	Osteoporosis	651	5.50%
8	Cerebrovascular diseases	556	4.70%
9	Glaucoma or cataracts	402	3.40%
10	Chronic bronchitis	400	3.40%
11	Deaf	282	2.40%
12	Neurological disorders	135	1.10%
13	Kidney disease	100	0.80%
14	Liver disease	69	0.60%
15	Cancer/Tumor	67	0.60%
16	Prostatic diseases	66	0.60%
17	Urinary system diseases	65	0.60%
18	Tuberculosis	34	0.30%
19	Emotional and mental issues	19	0.20%
20	Reproductive system diseases	10	0.10%

Table 3 Binary Logistic Regression Estimating Depressive Symptoms

Variables	Unadjusted OR (95% CI)	P	AOR (95% CI)	P
Number of Chronic Diseases	1.628 (1.54, 1.72)	<0.0001	1.655 (1.56, 1.75)	<0.0001
Living conditions	0.563 (0.46, 0.69)	<0.0001	0.684 (0.55, 0.85)	0.019

residence educational period and marital status), the analysis found that for each additional chronic disease, the risk of depressive symptoms increased by 66.1% (adjusted OR=1.661, 95% CI: 1.57, 1.76). The risk of depressive symptoms in older adults living alone is 31.6% lower than that in older adults cohabiting (adjusted OR = 0.684, 95% CI: 0.60, 0.96).

Causal Mediation Analysis

Table 4 shows the four-way decomposition analysis results examining the mediating role of chronic disease count. The analysis demonstrated that: (1) controlled direct effects (CDE) accounted for 71.64% of the total effect ($\beta = 0.384$, 95%

Table 4 The Role of the Number of Chronic Diseases in the Association Between Living Alone and Depression: a Four-Way Decomposition Analysis

	Excess RR (95% CI)	Proportion Attributable (%)	P
CDE	0.275 (0.011, 0.539)	71.64%	0.041
INTref	0.060 (-0.174, 0.293)	15.56%	0.616
INTmed	0.003 (-0.0201, 0.028)	0.89%	0.786
PIE	0.046 (0.005, 0.086)	11.91%	0.026
Total effect	0.384 (0.058, 0.709)		0.021

Notes: Analysis adjusted for age, gender, education level, marital status.

Abbreviations: CI, confidence interval; CDE, controlled direct effect; INTmed, mediated interaction; INTref, reference interaction; PIE, pure indirect effect; Total effect, CDE + INTref + INTmed + PIE.

CI: 0.058, 0.709); (2) reference interaction effects (INTref) represented 15.56% ($\beta = 0.060$, 95% CI: -0.174 , 0.293); (3) mediated interaction effects (INTmed) comprised 0.89% ($\beta = 0.003$, 95% CI: -0.020 , 0.028); and (4) pure indirect effects (PIE) explained 11.91% ($\beta = 0.046$, 95% CI: 0.005 , 0.086). While both the total effect and PIE reached statistical significance, neither INTref nor INTmed showed significant effects, with minimal effect sizes observed.

Discussion

The four-way decomposition analysis revealed that the effect of living alone on depression was predominantly mediated by a controlled direct effect (CDE). However, chronic disease quantity perception did not have a significant effect on the connection between living alone and depression. As a mediator, the total effect of the number of chronic diseases on the effect of living alone on depression was 11.91%.

The health problems of older adults living alone are characterized by a complex mix of physical-psychological and social factors. Lack of family support³³ makes older adults living alone more susceptible to social isolation, and their ability to function in their daily lives may be compromised^{34,35} which may lead to unhealthy lifestyle habits (lack of exercise and irrational diet).^{33,36–38} In addition, poorer economic status further exacerbates their feelings of loneliness and helplessness, making those who live alone more likely to suffer from depression than those who do not live alone.²¹ Older adults living alone contribute to feelings of loneliness due to reduced socialization and limitations in daily functional living.^{37,39} Particularly for older adults who are unmarried, childless, or away from family,^{10,40} the lack of family support creates an emotional void, which in turn increases the risk of depressive symptoms and negatively impacts overall health and quality of life. Furthermore, depression itself may exacerbate physical health problems, creating a vicious cycle. In the context of Chinese society, where family responsibilities are emphasized,⁴¹ the traditional family support model is facing significant challenges due to rapid urbanization and changes in family structure, particularly in rural areas. Older adults in rural areas, who often rely on their children for care,⁴² are especially affected by the weakening of intergenerational support systems, leading to a more severe experience of living alone.

The state of living alone may trigger a series of chain reactions. On the one hand, loneliness leads to feelings of loneliness and isolation,^{37,43} which not only affects the emotional well-being of older adults who live alone, but may also alter the structure of regions of the brain such as the superior frontal gyrus and the amygdala,⁴⁴ changes that can increase the occurrence of depressive symptoms.⁴⁵ On the other hand, vascular function and mood regulation are affected through physiological pathways such as activation of the stress response (elevated activity of the hypothalamic-pituitary-adrenal axis) and dysregulation of the immune system (increased pro-inflammatory markers).^{46,47} These physiological changes not only add to the physical burden, but may also exacerbate the emergence and development of depressive symptoms. In addition, older adults living alone often face decreased sleep quality due to loneliness, a change that affects their mental health.^{48,49} Sleep disorders are not only a direct consequence of loneliness, but may further affect mood regulation by interfering with the dopamine system in the brain.^{50,51} When sleep problems coexist with mood symptoms, depression tends to present longer and more severe episodes accompanied by a higher risk of relapse.⁵²

Although a significant correlation exists between solitary living and depressive symptoms, not all older adults who live alone experience depression. Individual characteristics, coping strategies, and the availability of social support systems may all influence the strength of this relationship.

The findings of this study demonstrate that the number of chronic diseases significantly mediates between living alone and depressive symptoms, accounting for 11.91% of the variance. People with chronic diseases are more likely to experience depression, and this risk increases with the number of diseases.^{25,26,53}

Older adults living alone, due to a lack of social support, are more prone to developing multiple chronic diseases, which increases their physical and psychological burden and raises the risk of depression. These diseases are often accompanied by increased inflammation, which affects immune system function and further exacerbates depression.^{28,54–57}

Other challenges faced by older adults living alone include a lack of necessary medical care, financial support, and social interactions in disease management and daily life,²⁹ which leads to lower treatment adherence.³⁴ Chronic diseases in older adults are typically long-lasting, difficult to cure, and prone to relapse, often requiring long-term or lifelong treatment. This increases financial pressure and mental stress,^{27,58} the prolonged presence of chronic diseases exacerbates the difficulties, increases their

healthcare burden, and reduces their quality of life.⁵⁹ Several commonly used medications, such as ACE inhibitors, beta-blockers, and corticosteroids, have also been associated with the onset or exacerbation of depressive symptoms.⁶⁰

In conclusion, the number of chronic diseases is a mediator for living alone and depression. Living alone indirectly raises the risk of depression in older adults by increasing the emergence and accumulation of chronic diseases, and the burden of chronic diseases worsens depression due to its dual physical and psychological effects.

Therefore, attention should be given to the dual impact of living alone and chronic diseases on depression, especially the loneliness and social isolation caused by living alone. While managing chronic diseases, it is necessary to combine psychological interventions, pay attention to the living conditions of the older adults, and identify and treat depression early. Strengthening social support, providing emotional comfort, and increasing social opportunities can effectively reduce the risk of depression and improve the quality of life for older adults living alone. It is recommended to include mental health assessments in the routine care for older adults living alone, especially those with multiple chronic diseases, to reduce the disease burden, promote early detection and intervention of depression, improve prognosis, and enhance the well-being of older adults living alone.

The current study focused on the association between the number of chronic diseases and depressive symptoms in older adults living alone, as well as potential mediation mechanisms, however it has several limitations. First, the study's cross-sectional design made it impossible to show a causal association between living alone, the number of chronic diseases, and depressive symptoms. Second, the study relied on participants' self-reported information about chronic diseases, which could have been skewed by memory bias, leading to false reporting. Furthermore, self-reports did not accurately reflect the severity and management of chronic diseases, which could have impacted the assessment of depressed symptoms. Finally, this study did not account for other potential confounders that may influence depression symptoms, which could have an impact on the findings' accuracy.

Conclusion

There is a significant association between living alone and depressive symptoms. The number of chronic diseases plays a mediating role between living alone and depressive symptoms, but its proportion is relatively small. Therefore, clinical interventions should focus more on strengthening social support and providing emotional support, rather than just focusing on the management of chronic diseases. By enhancing social support systems, providing emotional comfort, and increasing social opportunities, the risk of depression among older adults living alone can be effectively reduced, and their quality of life can be improved. However, the cross-sectional design of this study limits the interpretation of causal relationships. Future research should consider adopting a longitudinal study design to better understand the dynamic relationships between living alone, chronic diseases, and depression. In the process of policy implementation, comprehensive medical services that meet the physical and psychological needs of older adults living alone should be provided to promote healthy aging.

Data Sharing Statement

The datasets used and/or analyzed in the present study are available from the corresponding author on reasonable request.

Ethics Declarations

The study was approved by the Ethics Committee of The Second Affiliated Hospital of Guangxi Medical University (No. 2023-KY0905). All experimental protocols were approved by the Ethics Committee. All participants signed a written informed consent form. All human studies were reviewed by the appropriate ethics committees and conducted in accordance with the ethical standards set forth in the appropriate version of the Declaration of Helsinki.

Acknowledgments

The authors would like to thank all of the older adults and researchers who participated in this survey.

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.

Funding

This study was supported by the Guangxi Philosophy and Social Science Research Project (22FRK004).

Disclosure

The authors declare no competing interests.

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