

The Association Between Social Isolation and Medication Adherence Among Chinese Older Adults With Chronic Diseases: Serial Mediation of Social Support and Loneliness

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Abstract

Background Medication adherence is essential for chronic disease management among older adults. Previous studies have shown significant links among social isolation, social support, loneliness, and medication adherence, yet most were based on cross-sectional designs.

Purpose We conducted a longitudinal cohort study among Chinese older adults with chronic diseases to explore the mediating effects of social support and loneliness in the association between social isolation and medication adherence.

Methods This study followed a cohort of 797 older adults with chronic diseases in China from 2022 to 2023. The serial mediation model was examined via bootstrapping techniques to evaluate the mediating effect of social support and loneliness in the association between social isolation and medication adherence.

Results From baseline to follow-up, there were significant decreases in social support (from 26.6 ± 6.2 to 23.5 ± 6.7) and medication adherence (from 6.7 ± 1.2 to 6.0 ± 1.5) and significant increases in social isolation (from 1.8 ± 1.3 to 2.5 ± 1.4) and loneliness (13.2 ± 4.1 to 23.5 ± 6.7), all with $p < .001$. A serial mediation model was confirmed, where social support and loneliness serially and partially mediated the association between social isolation and medication adherence (total effect $c = -0.216$, 95% CI = -0.296 to -0.136 ; direct effect $c' = -0.094$, 95% CI = -0.171 to -0.017 ; total indirect effect $ab = -0.122$, 95% CI = -0.179 to -0.070).

Conclusions Our findings yield critical insights into the relationship between social isolation and medication adherence through various mediating mechanisms. These findings hold significant implications for devising psychosocial interventions to enhance medication adherence among older adults with chronic diseases, underscoring the pivotal role of bolstering social support and alleviating loneliness.

Lay summary

This study investigated the relationship between social isolation, medication adherence, and psychosocial factors (social support and loneliness) in Chinese older adults with chronic diseases. We observed decreases in social support and medication adherence and increases in social isolation and loneliness from baseline to follow-up. The findings revealed that social support and loneliness sequentially and partially mediated the association between social isolation and medication adherence. These results highlight the importance of psychosocial interventions to improve medication adherence among older adults by enhancing social support and addressing feelings of loneliness. This study contributes to our understanding of the complex factors influencing medication adherence in this population and offers insights for designing effective interventions.

Keywords Medication adherence · Social isolation · Social support · Loneliness · Older adults · Chronic disease

Introduction

Chronic diseases represent a significant global health concern, projected to contribute to 70.0% of global deaths and 56.0% of the worldwide disease burden by 2030 [1, 2]. A primary strategy for chronic disease control is medication, which has been demonstrated to manage the symptoms of chronic diseases and associated problems effectively. Abundant evidence suggests medication adherence can reduce hospitalizations and emergency department (ED) visits, improve patient health outcomes, and decrease healthcare expenses [3].

Medication adherence refers to “the extent to which a patient’s behavior in medicine-taking corresponds with agreed recommendations from a healthcare provider” [4]. Despite robust evidence showing the value of taking medications as prescribed, poor medication adherence remains a global challenge, with an estimated 50% of the worldwide population with chronic diseases having poor medication adherence [4]. Poor medication adherence may lead to adverse clinical outcomes and increased healthcare costs, and a recent systematic review and meta-analysis showed that medication

non-adherence was significantly associated with all-cause hospitalization and mortality in older people [5].

Social isolation is characterized by reduced size and diversity of social networks and decreasing frequencies of contact with family and friends [6]. Social isolation is one of the most common and severe social problems among older adults (defined as those aged ≥ 60) with chronic diseases. Valtorta et al.'s [7] systematic review and meta-analysis of longitudinal studies on social isolation in high-income countries published up until May 2015 reported an estimated prevalence ranging from 2.8% to 77.2%. Cudjoe et al. [8] constructed a typology of social isolation using data from the US National Health and Aging Trends Study (NHATS). They found that in the year of 2011, 24% of community-dwelling adults aged ≥ 65 were socially isolated, and 4% were severely socially isolated, defined as those who were living alone, had nobody to talk about essential things in the past year, and attended no religious services or social activities in the past month [8].

Social isolation is a well-documented risk factor for medication non-adherence among older adults with chronic diseases, with studies showing that older adults with higher levels of social isolation were less likely to adhere to their prescribed medications [9]. Multiple mechanisms may explain the link between social isolation and medication adherence, among which social support and loneliness are the two most widely reported factors. Social support involves tangible and intangible support that people get from their societal relationships, including family, friends, and colleagues [10]. Social support can promote older adults' medication adherence through tangible support, such as the provision of medication reminders, preparation, and monitoring, as well as intangible support, such as the expression of love and care about their health and medicine-taking behaviors [11, 12]. Numerous studies underscore that social isolation can erode an individual's social support, leading to reduced or even lack of access to tangible and intangible support for medication adherence [6, 13, 14]. Older adults with social isolation have limited social networks and may face difficulties accessing adequate social support, thereby heightening the risk of medication non-adherence [9].

Loneliness refers to an emotional state where individuals subjectively perceive a deficiency in social connection and interaction and is characterized by emotional isolation and a sense of being socially distanced [15]. Loneliness frequently arises from the gap between people's social expectations and their real-life experiences [16]. Social isolation can lead to loneliness both directly and indirectly through reduced social support [17]. In addition, loneliness can adversely impact health behaviors in circumstances where individuals perceive hurdles in establishing meaningful social connections, leading to poor medication adherence [18, 19]. Older adults with social isolation have reduced social networks and interactions, leading to decreased social support, which can result in loneliness and make them feel excluded, neglected, and unsafe due to a lack of attention, care, and support from their limited social networks [20]. Such feelings may introduce implicit hypervigilance for social threats in the environment, leading to increased stress levels, thus eliciting adverse maladaptive behaviors such as medication non-adherence [9]. Therefore, restricted social interaction can lead to diminished social support, potentially inducing loneliness and further leading to medication non-adherence [20].

Several studies [9, 21–24] underscored significant links between social isolation, social support, and loneliness in chronic disease management among older adults. For example, Lu et al. [9] employed a mixed-methods design with integrated theory and validated cross-sectional study in six districts of Taiyuan, China. They found that low social support mediated the association between social isolation and suboptimal medication adherence among older adults [9]. Öksüz et al. [24] conducted a cross-sectional study among 119 patients with ankylosing spondylitis. They found that nonadherent patients had higher levels of loneliness and lower levels of social support than adherent patients [24]. A systematic review of observational studies has identified three domains of psychological determinants (including knowledge, beliefs about consequences, and emotions) that most influence stroke survivors' medication adherence [25]. However, most previous findings rely heavily on cross-sectional designs, which can neither reflect the temporal evolution of variables nor establish sequential occurrences among independent, mediating, and dependent variables required for mediation analysis. Christiansen et al. [21] conducted a 5-year follow-up study and found that loneliness and social isolation were independently associated with cardiovascular disease (CVD) and diabetes mellitus Type 2 (T2D). In addition, loneliness and SI had an indirect effect on CVD and T2D through both baseline psychological and behavioral factors [21]. However, it remains unknown how older adults' social isolation changes over time and how these changes affect their social support and feelings of loneliness and ultimately affect their medication adherence [25]. A dynamic understanding of the intricate interconnections among these longitudinal variables is crucial to exploring the underlying mechanisms of the association between social isolation and medication adherence and to guide future interventions to break such a link and improve medication adherence.

To fill in the research gap, we conducted a 1-year longitudinal study. We prospectively followed up a cohort of 797 Chinese older adults with chronic diseases, with the following specific goals: (i) to investigate the temporal changes of social isolation, social support, loneliness, and medication adherence; (ii) to explore the association between social isolation and medication and whether such an association was serially mediated by social support and loneliness. We hypothesized that older adults would experience increased social isolation and loneliness and decreased social support and medication adherence over time. In addition, social support and loneliness would serially mediate the association between social isolation and medication adherence.

Methods

Study methods and results are reported following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement for cohort studies.

Study Design and Participants

The study's sample originated from the central hospital of Shaoyang in Hunan Province, China. Located in the southwest of central Hunan, Shaoyang is a prefecture-level city encompassing 20,824 km² and had a permanent population of 6,417,800 as of the end of 2022. Established in 1946, the central hospital of Shaoyang is the largest tertiary class A general hospital in central and southwest Hunan, offering

integrated services in medical treatment, education, research, prevention, healthcare, and rehabilitation.

For this study, a whole sampling approach was employed, enrolling all eligible older adults with chronic diseases who visited the hospital's outpatient departments from July 1 to 15, 2022. The presence of a chronic disease was determined based on a combination of medical diagnostic records and self-reported questionnaires. First, patients with prespecified International Classification of Diseases codes (ICD codes) for a range of chronic diseases were identified through the electronic medical system by clinicians at the research hospital. The patients were then referred to our research team for the questionnaire survey, where they were further asked about whether they had ever been diagnosed with any chronic disease such as hypertension and diabetes. This dual approach enhances the comprehensiveness and accuracy of the data, ensures the reliability of the research results, and contributes to a comprehensive understanding of the health status of the respondents from an objective and personal perspective.

The inclusion criteria of participants were: (i) being aged ≥ 60 years and residing in one of the three districts under Shaoyang's jurisdiction (Shuangqing, Daxiang, or Beita District), (ii) having at least one chronic disease, such as hypertension, diabetes, coronary heart disease, or chronic obstructive pulmonary disease (COPD), etc., (iii) undergoing treatment with medication prescribed by a clinician for at least 3 months, and (iv) capable of reading, writing, and communicating in Chinese. Those who were unable to complete the questionnaire survey due to severe physical or mental impairments were excluded.

The sample size was calculated using McNemar's test formula for longitudinal study:

$$n = (Z_{\alpha/2} + Z_{\beta})^2 \times [p_1 \times (1 - p_1) + p_2 \times (1 - p_2)] / (p_1 - p_2)^2,$$

where $Z_{\alpha/2} = 1.96$ for a 95% confidence level and $Z_{\beta} = 0.84$ for a power of 80%. p_1 (the baseline non-adherence rate) was estimated to be 35% based on a recent study in China [26] and p_2 (the follow-up non-adherence rate) was estimated to be 45% as medication non-adherence among older adults would increase over time, especially without effective interventions [27]. Based on the formula, the required sample size was approximately 372. Considering an anticipated dropout or loss to follow-up rate of 20%, we expanded the sample size to 465. This sample size ensures the study has adequate power to detect significant differences in medication adherence.

Procedure

This study was carried out as a social practice project by students from the 2020 cohort majoring in ideological and political education at the School of Marxism, Shaoyang University. It formed a part of the curriculum for two compulsory courses for the students: "Social Investigation and Research Methods" in 2022 and "Social Survey and Research Methods" in 2023. Students need to complete data collection in both courses in order to get their course credits. The research team comprised 46 students from the program who received standardized training in interviewing and questionnaire techniques prior to commencing the study. These students were subsequently divided into groups and assigned to various outpatient departments handling chronic diseases to collect samples during outpatient services.

This study received ethical approval from the Ethics Review Committee of Guangxi Normal University ([2022]0610001) and adhered to ethical standards and requirements in data

collection, with additional written consent from the central hospital of Shaoyang. The baseline survey was conducted in July 2022 as the final project of the course "Social Investigation and Research Methods." Eligible respondents, identified initially by clinic nurses, were informed about the study by the nurses and then referred to our research team. The team thoroughly explained the study's objectives, methodology, benefits, and risks to the participants, ensuring their privacy and anonymity. Informed consent was obtained from all participants before the study commenced. Data collection was conducted in a designated interview room through face-to-face questionnaires. Post-interview, contact details of patients or their family members were recorded for subsequent follow-up. Initially, 840 older adults with chronic diseases were enrolled at the baseline stage, with 820 completing the questionnaire, resulting in a 97.6% response rate.

The follow-up survey was conducted in July 2023 as the final project for the course "Social Survey and Research Methods" of the same group of students who reached out to the older adults under their management at the baseline survey. Upon obtaining consent, face-to-face questionnaires were administered at the patients' designated locations. Among the 820 participants enrolled in the baseline survey, a total of 23 individuals were unable to participate in the follow-up due to health reasons. Consequently, 797 participants successfully completed the follow-up survey, yielding a high response rate of 97.2%. The investigators accurately matched the data from both surveys using the pre-recorded identification numbers. Both surveys used the same questionnaires to collect participants' demographic information, medication adherence, social isolation, social support, and loneliness, each described below.

Measures

Basic information

A self-designed information sheet was employed to gather participants' demographic information, including gender, resident type, marital status, living arrangement, educational level, monthly income, number of children, and provision of long-term care for grandchildren. Additionally, we captured data on disease-related characteristics, such as the frequency and duration of chronic diseases.

Medication adherence

Medication adherence was assessed by the Morisky Medication Adherence Scale (MMAS-8) [28]. It comprises seven "yes" (1 point) or "no" (0 point) items and one item rated on a 5-point Likert scale ranging from 0 to 4. A scoring algorithm was applied to item 8 to get a total score ranging from 0 to 8, which was further categorized as low (<6), medium (6–7), and high adherence ($=8$). In this study, the Cronbach's alpha coefficient for the MMAS-8 was 0.81, indicating good internal consistency.

Social isolation

Social isolation was assessed by the Social Isolation Index (SII) [29]. It includes five items, and the total score ranges from 0 to 5, with a higher score indicating a higher level of social isolation. A cutoff of 2 was used to distinguish between those with lower (≤ 2) and higher (>2) levels of social isolation. In this study, the Cronbach's alpha of SII was 0.89, indicating good internal consistency.

Social support

Social support was assessed by the Social Support Rating Scale (SSRS) [30], one of the most widely used social support tools with well-established reliability and validity. It includes 10 items under three dimensions: objective support, subjective support, and support utilization. The total score ranges from 12 to 66, with a higher score indicating greater perceived social support. The score was further categorized into three levels, meaning low (≤ 22), moderate (23–44), and satisfactory (45–66) social support. In this study, the Cronbach's alpha coefficient for the SSRS was 0.88, indicating good internal consistency.

Loneliness

Loneliness was assessed using the Simple Loneliness Scale (ULS-6) [31]. It consists of six questions, each scored from 1 (never) to 4 (often). The total score ranges from 6 to 24, with a higher score indicating a higher degree of loneliness. In this study, the Cronbach's alpha coefficient of the ULS-6 was 0.88, indicating good internal consistency.

Statistical Analyses

All data analyses were conducted using the SPSS 26.0. continuous variables were expressed as means \pm standard deviations, while categorical data were presented as numbers and percentages. Pearson's Chi-square test and paired T-test were used to compare the patients' characteristics from baseline and follow-up. Pearson correlation analysis was conducted to investigate the associations among key variables. The serial mediation analysis was carried out using SPSS PROCESS v.4.1 macros (Model 6) [32], with social isolation (X) as the independent variable, medication adherence (Y) as the dependent variable, and social support and loneliness as two consecutive mediators, while accounting for all sociodemographic and clinical characteristics as covariables. A bootstrapping method consisting of 5,000 samples was used to establish the significance of these mediators. According to Hayes [32], a 95% bootstrap confidence interval (CI) excluding zero and a $p < .05$ indicated statistical significance.

Results

Sample Characteristics and Changes

The study included 797 participants whose characteristics are outlined in Table 1. At baseline, the participants had a mean age of 69.7 ± 7.9 years old, with slightly more females than males (52.7% vs. 47.3%). Most were rural dwellers (60.2%), married (61.9%), living with someone (86.2%), had two or fewer children (63.1%), and were long-term caregivers for their grandchildren (57.3%). Additionally, 41.7% had only attained primary school education, and 41.4% had a monthly income below 2,000 Yuan. Multimorbidity, defined as having two or more chronic diseases, was present in 13.6% of the participants whose average disease duration was 27.2 ± 13.2 months. At follow-up, no significant changes in these characteristics were observed (all $p > .05$).

However, the four key indicators showed significant changes from baseline to follow-up, with significant decreases in social support (from 26.6 ± 6.2 to 23.5 ± 6.7) and medication adherence (from 6.7 ± 1.2 to 6.0 ± 1.5) and significant increases in social isolation (from 1.8 ± 1.3 to 2.5 ± 1.4) and loneliness (13.2 ± 4.1 to 23.5 ± 6.7), all with $p < .001$.

Correlations on the key variables

Table 2 demonstrates the correlation coefficients between baseline social isolation and social support, loneliness, and medication adherence at follow-up. All correlations were statistically significant and below 0.80, thus excluding multicollinearity [33]. Specifically, baseline social isolation demonstrated a negative correlation with both social support ($r = -.728$, $p < .01$) and medication adherence ($r = -.702$, $p < .001$) at follow-up. Conversely, it showed a positive correlation with loneliness at follow-up ($r = .606$, $p < .01$). Additionally, medication adherence at follow-up was positively correlated with baseline social support ($r = .744$, $p < .01$) and negatively correlated with baseline loneliness ($r = -.765$, $p < .01$). Furthermore, baseline social support and loneliness at follow-up were found to be negatively correlated with each other ($r = -0.598$, $p < .01$).

Serial Mediation Model Analysis

Figure 1 and Table 3 delineate the total, direct, and indirect influences of social isolation on medication adherence, mediated through social support and loneliness. The total effect of social isolation on medication adherence was significant ($c = -0.216$, 95% CI = -0.296 to -0.136). When two mediators were added, the direct effect of social isolation on medication adherence decreased but remained significant ($c' = -0.094$, 95% CI = -0.171 to -0.017). The total indirect effect of social isolation on medication adherence was significant ($ab = -0.122$, 95% CI = -0.179 to -0.070). Both mediators, social support and loneliness, showed a significant effect on medication adherence, as represented by corresponding mediator paths ($a1b1 = -0.056$, 95% CI: -0.092 to -0.025 ; $a2b2 = -0.046$, 95% CI: -0.083 to -0.012). Furthermore, a significant indirect effect was found for social isolation through social support and loneliness ($a1a3b2 = -0.020$, 95% CI = -0.035 to 0.009). Social isolation led to low social support, which likely triggered loneliness and thus predicted low medication adherence. Among the three mediation pathways, social support accounts for the majority of the mediation effect (45.9%), followed by loneliness (37.7%), and a combination of social support and loneliness (16.4%).

Discussion

Summary of the Findings

This longitudinal research followed a cohort of 797 older adults with chronic diseases from 2022 to 2023 to examine the changes and associations among four key variables: social isolation, social support, loneliness, and medication adherence. Compared to the baseline, participants experienced significant declines in social support and medication adherence and significant increases in social isolation and loneliness at follow-up. Through the application of a serial mediation model, we found a significant association between social isolation and medication adherence, with social support and loneliness partially and serially mediating this impact. Moreover, social support accounted for the largest proportion of the total indirect effect of Social isolation on medication adherence. Our findings stressed the essential role of psychosocial factors in influencing medication adherence behaviors, providing important implications for future comprehensive and targeted psychosocial interventions to improve medication adherence among older adults with chronic diseases.

Table 1 Changes of Sample Characteristics and Key Indicators from Baseline to Follow-up ($n = 797$)

Variables	Baseline data n (%) / $\bar{x} \pm S$	Follow-up data n (%) / $\bar{x} \pm S$	χ^2	p values	Variables	Baseline data n (%) / $\bar{x} \pm S$	Follow-up data n (%) / $\bar{x} \pm S$	χ^2/t	p values
Age (years)	69.7 \pm 7.9	70.7 \pm 7.9			Number of children	2.2 \pm 0.9	2.2 \pm 0.9		
Gender					≤ 2	503 (63.1)	503 (63.1)		
Male	377 (47.3)	377 (47.3)			> 2	294 (36.9)	294 (36.9)		
Female	420 (52.7)	420 (52.7)			Caring for grandchildren				
Resident type					Yes	457 (57.3)	473 (59.3)	0.66	.416
Urban	317 (39.8)	317 (39.8)			No	340 (42.7)	324 (40.7)		
Rural	480 (60.2)	480 (60.2)			Multimorbidity				
Marital status					Yes	108 (13.6)	136 (17.1)	3.79	.051
In marriage	493 (61.9)	487 (61.1)	0.11	.991	No	689 (86.4)	661 (82.9)		
Unmarried	12 (1.5)	12 (1.5)			Duration of disease/month	27.2 \pm 13.2	39.2 \pm 13.2		
Widowed	244 (30.6)	250 (31.4)			Social isolation				
Divorced	48 (6.0)	48 (6.0)			Low	539 (67.6)	347 (43.5)	93.68	<.001
Living condition					High	258 (32.4)	450 (56.5)		
Live alone	110 (13.8)	108 (13.6)	0.18	.981	Social isolation score	1.8 \pm 1.3	2.5 \pm 1.4	-21.53	<.001
Couple living together (empty nest)	206 (25.8)	200 (25.1)			Social support ^a				
Living with children	445 (55.9)	453 (56.8)			Low	202 (25.3)	350 (43.9)	60.70	<.001
Live with others	36 (4.5)	36 (4.5)			Moderate	595 (74.7)	447 (56.1)		
Education level					Social support score	26.6 \pm 6.2	23.5 \pm 6.7	23.67	<.001
Primary school	332 (41.7)	332 (41.7)			Loneliness	13.2 \pm 4.1	14.0 \pm 3.9	-6.91	<.001
Junior high school	232 (29.1)	232 (29.1)			Medication adherence				
High school or technical secondary school	123 (15.4)	123 (15.4)			Low	148 (18.6)	244 (30.6)	36.91	<.001
Junior college	72 (9.0)	72 (9.0)			Medium	419 (52.6)	393 (49.3)		
Undergraduate	38 (4.8)	38 (4.8)			High	230 (28.9)	160 (20.1)		
Family monthly income (RMB)					Medication adherence score	6.7 \pm 1.2	6.0 \pm 1.5	27.33	<.001
<2,000	330 (41.4)	318 (39.9)	0.97	.617					
2,001–3,000	126 (15.8)	140 (17.6)							
$\geq 3,001$	341 (42.8)	339 (42.5)							

^aThe social support scores ranged from 12 to 44 points, with none falling into the high social group (45–66 range).

Table 2 Pearson's Correlations Among Study Variables

	Follow-up social isolation	Follow-up social support	Follow-up loneliness	Follow-up medication adherence
Baseline social isolation	0.752*	-0.728*	0.606*	-0.702*
Baseline social support		0.739*	-0.598*	0.744*
Baseline loneliness			0.663*	-0.765*
Baseline medication adherence				0.787*

* $p < .01$.

Social Isolation and Medication Adherence

Consistent with previous research [9], our study showed a significant association between social isolation and medication adherence, indicating social isolation as an important

contributing factor to medication non-adherence. Managing chronic diseases necessitates older adults to take charge of their well-being, where medication adherence is paramount to effective self-management [34]. However, older adults

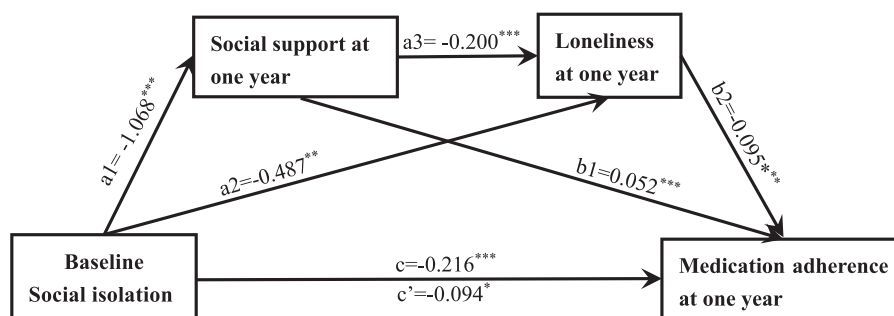


Fig. 1. Schematic diagram of the serial mediation model illustrating the direct effects in the relationships among social isolation, medication adherence, social support, and loneliness. * $p < .05$, ** $p < .01$, *** $p < .001$.

Table 3 Total, Direct, and Indirect Effects of Social Isolation Involvement on Medication Adherence^a

Path	<i>B</i>	<i>SE</i>	LLCI	ULCI
Total effect (<i>c</i>)	-0.216	0.041	-0.296	-0.136
Direct effect (<i>c'</i>)	-0.094	0.039	-0.171	-0.017
Total indirect effects (<i>ab</i>)	-0.122	0.028	-0.179	-0.070
Baseline social isolation → Follow-up social support → Follow-up medication adherence (<i>a1b1</i>)	-0.056	0.017	-0.092	-0.025
Baseline social isolation → Follow-up loneliness → Follow-up medication adherence (<i>a2b2</i>)	-0.046	0.018	-0.083	-0.012
Baseline social isolation → Follow-up social support → Follow-up loneliness → Follow-up medication adherence (<i>a1a3b2</i>)	-0.020	-0.007	-0.035	-0.009

CI, confidence interval; LLCI, low limit confidence interval; ULCI, upper limit confidence interval.

^aNumber of bootstrap samples for bias-corrected bootstrap CIs: 5,000.

living with social isolation face extraordinary challenges to self-management due to a lack of social networks and support to facilitate healthy behaviors [35]. The influence of social isolation on medication adherence in older adults with chronic diseases is anchored in multiple theories and research paradigms. Primarily, social cognitive theory (SCT) underscores the significant role of the social milieu in influencing behavior [36], asserting that social isolation may curtail patient access to vital reinforcements and encouragement [37], thereby impacting medication schedules, self-drive, and regimen regulation. Next, the health belief model (HMB) posits that social isolation could deepen the patient's appraisal of disease risk and intensity, and undermine their faith in, and effectiveness assessment of pharmaceutical therapies [38], thereby influencing medication adherence. Concurrently, psychosocial factors are also vital; social isolation can incite psychological distress and emotional turmoil, and aligns closely with feelings of loneliness and depression [39], which, in turn, disrupts positive attitudes and confidence in treatment. Social isolation might also compromise access to crucial social support systems for the patient [23], which stands critical in amplifying individual behavior and maneuvering disease-related challenges.

The Serial Mediating Effect of Social Support and Loneliness

Our research confirmed the serial mediating roles of social support and loneliness in the association between social isolation and medication adherence, with social support alone playing the largest mediating effect. Notably, none of the participants in our study had a high level of social support

(SSRS score >44) during the two research periods, signifying persistently low social support among this population. The strikingly low levels of social support in our study warrant further investigation in other samples of older adults with chronic illnesses in other studies. Social support significantly influences the management of chronic diseases and the lives of older adults by bolstering medication adherence [40]. It offers emotional solace, health guidance, and practical assistance, substantially enhancing patients' self-efficacy in health management [41]. Additionally, social support networks assume a supervisory role, facilitating medication adherence reminders, schedule management, and overcoming challenges.

Moreover, loneliness exhibited an upward trend over time, likely attributed to diminished social support in individuals experiencing heightened social isolation. Given that social support is a well-recognized protective factor against loneliness, these observations align with established patterns. Older adults often encounter transitions in their social roles [42], such as retirement or their children's independence, leading to diminished social interactions, heightened social isolation, an absence of social support, and intensified loneliness. Moreover, the challenges posed by chronic illnesses can evoke feelings of helplessness and depression among older adults, compelling them to curtail social engagements due to health complexities, thereby exacerbating their lack of social support and escalating loneliness [43]. Loneliness is significantly associated with social isolation and social support, as diminished social connections breed feelings of disconnection, reducing social support and amplifying loneliness [18]. Therefore, social isolation leads to a reduction in social support, and an increase in loneliness,

and collectively diminishes the inclination of older patients with chronic diseases to seek treatment, ultimately hindering their medication adherence.

Additionally, motivational factors also play an essential role in the medication adherence and self-care of older adults requiring long-term treatment [44, 45]. Patients with chronic illnesses need to maintain their motivation to adhere to medication regimens and other recommendations over a long time [44, 45]. They may experience natural fluctuations in their engagement with the treatment, and these critical moments can be significantly more challenging for people having a limited social network or a sense of loneliness, making them more likely to disengage from the treatment. Therefore, future interventions targeting improving older adults' medication adherence via improving social support and loneliness should also take motivational factors into account to achieve the maximal effects.

Limitations

This study presents several limitations. First, our sample was recruited from a tertiary hospital located in an urban city of Hunan Province and may not represent patients from rural areas and other parts of China. Future studies should consider multi-center sampling to recruit chronic patients from various regions, such as the community, rural areas, and other parts of China, to get a more representative sample. Second, the reliance on self-reported data for medication adherence introduces potential biases, such as recall and social desirability biases, which may lead to inaccuracies in depicting actual adherence behaviors. This method also overlooks the complex nature of medication adherence, suggesting a need for future research to employ a combination of self-reported and objective measures, like pharmacy refill records, electronic medication tracking, or pill counts, for a more holistic and accurate assessment of older adults with chronic diseases. Third, the short follow-up period from 2022 to 2023 limits the study's ability to capture the long-term dynamics of the relationships between the key variables. We will continue our subsequent follow-ups for this cohort to provide more valuable insights into the long-term associations between social isolation and medication adherence via social support and loneliness. Fourth, the study did not account for other factors that may affect medication adherence, as indicated by the small magnitude of the total and indirect effects. Given that medication adherence is a complex behavior, future research may benefit from using a more complex model with multiple independent variables, mediators, and dependent variables to understand the mechanism of medication adherence more comprehensively. Fifth, the lack of mental/behavioral health variables and cognitive data may also limit a full exploration of factors influencing medication adherence. Future studies should add these variables to get a more comprehensive picture. Sixth, we did not distinguish patients with different clinical characteristics, such as various chronic disease diagnoses (diabetes vs. heart disease), when testing our mediation model. Future studies should test whether there would be any differences in the strength of the mediation pathways based on clinical characteristics. Finally, we did not explore the relationship between social support, loneliness, and other factors, such as age, gender, caring for grandchildren, and time elapsed since diagnosis or medical condition, which will be one of our following research topics.

Implications

Our study carries significant clinical, research, and policy implications to enhance medication adherence in older adults with chronic conditions, thereby improving their overall quality of life. From a clinical perspective, for patients with poor medication adherence, healthcare professionals may consider involving the patient's family members to provide medication-related support and care. Collectivism-oriented culture is deeply embedded in Chinese society, where family members play an essential role in the care and support of older adults with chronic illnesses [46]. Such an approach can indirectly improve medication adherence, optimizing treatment outcomes. From a research perspective, future research should delve deeper into the relationship between social isolation and medication adherence and include more mediating factors. Consideration might be given to expansive, long-term studies to explore the long-term dynamic changes of multiple factors and their influence on medication adherence, which can help guide comprehensive and targeted medication adherence interventions. From a political perspective, policymakers should focus on strengthening social support systems and fostering opportunities for social engagement to mitigate loneliness among older adults and improve medication adherence. Policies are needed to integrate psychosocial support into the healthcare systems to enhance the care quality of care for older adults with chronic illness.

Conclusions

In summary, our study aligns with previous research, underscoring the influence of social isolation on medication adherence, which was partially and sequentially mediated by social support and loneliness. Specifically, older adults with social isolation may have lower levels of social support, which may trigger loneliness, further leading to poor medication adherence. Our research expands the understanding of how social isolation affects medication adherence, illuminating its multifaceted mediation by social support and loneliness. These findings yield critical insights for both research and practical endeavors aimed at developing psychosocial interventions to enhance medication adherence, emphasizing the crucial role of improving social support and alleviating loneliness to enhance the management of chronic diseases among older Chinese adults.

Acknowledgments

This study was funded by the Philosophy and Social Science Foundation of Hunan Province (Grant No. 21YBA178), and we extend our gratitude to all the older adults with chronic diseases who participated in our survey. Additionally, we acknowledge the committed efforts of the 2020 cohort of ideological and political education students from Shaoyang University in recruiting respondents. Lastly, our thanks go to the medical staff at Shaoyang Central Hospital for their invaluable assistance in facilitating this study.

Compliance with Ethical Standards

Authors' Statement of Conflict of Interest and Adherence to Ethical Standards Authors Yong YU, Qianye Huang, Zheng REN, and Zhiwen OU declare that they have no conflict of interest. All procedures, including the informed consent

process, were conducted in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000.

Authors' Contributions Yong Yu (Conceptualization [lead], Data curation [lead], Formal analysis [lead], Investigation [equal], Methodology [lead], Project administration [equal], Resources [equal], Software [lead], Supervision [lead], Validation [lead], Writing – original draft [lead], Writing – review & editing [equal]), Qian Yue Huang (Data curation [equal], Investigation [lead], Methodology [equal], Resources [lead], Software [equal], Supervision [equal], Validation [equal], Writing – original draft [equal], Writing – review & editing [equal]), Zheng Ren (Conceptualization [lead], Data curation [lead], Investigation [lead], Methodology [lead], Project administration [lead], Resources [equal], Software [equal], Supervision [lead], Validation [equal], Visualization [equal], Writing – review & editing [lead]), and Zhiwen OU (Conceptualization [supporting], Data curation [supporting], Funding acquisition [lead], Project administration [supporting], Resources [supporting], Supervision [supporting], Validation [supporting], Visualization [supporting], Writing – review & editing [supporting])

Transparency Statements

Study registration: This study was not formally registered. **Analytic plan pre-registration:** The analysis plan was not formally pre-registered. **Data availability:** De-identified data from this study are not available in a public archive. De-identified data from this study will be made available (as allowable according to institutional IRB standards) by emailing the corresponding author. **Analytic code availability:** There is no analytic code associated with this study. **Materials availability:** Materials used to conduct the study are not publically available.

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