

Effects of Social Support on Medication Adherence Among Patients with Schizophrenia: Serial Multiple Mediation Model

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Purpose: This study aims to explore the serial mediating effect of stigma and depression on the association between social support and medication adherence.

Patients and Methods: A cross-sectional survey was undertaken in the Changning District of Shanghai using a five-part questionnaire from August to December 2023. A convenient sampling method was employed, and 35 patients with schizophrenia were invited from each of the 9 streets in Changning District to participate in the survey, resulting in a total of 305 valid questionnaires collected. The questionnaire measured social support, stigma, depression, medication adherence, and demographic characteristics. Data analysis involved descriptive statistics, independent samples t-tests, ANOVA, Pearson correlation analysis, and the bootstrap method.

Results: There was a direct and significantly positive association between social support and medication adherence ($\beta = 0.69$, $p < 0.001$). Moreover, increased levels of stigma ($\beta = -0.45$, $p = 0.013$) and depression ($\beta = -0.09$, $p = 0.017$) were both associated with a decline in medication adherence. Bootstrapping analysis revealed that the association between social support and medication adherence operated indirectly through stigma ($\beta = 0.11$, 95% CI: 0.03, 0.18). Additionally, social support was indirectly associated with medication adherence through depression ($\beta = 0.15$, 95% CI: 0.04, 0.30). Further analysis indicated that social support had an indirect association with medication adherence through both stigma and depression ($\beta = 0.04$, 95% CI: 0.01, 0.07).

Conclusion: Stigma and depression serially mediate the association between social support and medication adherence among patients with schizophrenia. This serial multiple mediation model underscores the importance of integrating social support interventions with psychological interventions aimed at reducing stigma and depression, thereby effectively enhancing medication adherence in patients with schizophrenia.

Keywords: social support, stigma, depression, medication adherence, schizophrenia

Introduction

Schizophrenia is a complex, heterogeneous behavioral and cognitive syndrome, characterized by persistent or recurrent episodes of psychosis.^{1,2} The lifetime prevalence of schizophrenia ranges from 0.3% to 0.7% globally,³ with approximately 24 million individuals diagnosed with schizophrenia.⁴ In China, the reported lifetime prevalence rate of schizophrenia is 0.6%, affecting approximately 8 million individuals.⁵ Continuous long-term treatment is essential for the effective management of schizophrenia, typically involving a combination of antipsychotic medications and psychosocial interventions.^{6,7} Medication adherence is considered as the strongest predictor of relapse in patients with

psychosis, where non-adherent patients estimated to have a 3–5 times higher risk of relapse compared to adherent patients.^{8–10} However, current studies indicate that the rates of medication non-adherence among patients with schizophrenia range from 40% to 70%.^{8,11–13} This results in frequent relapses in patients with schizophrenia and may also contribute to an increased potential for aggression and dangerous behavior during periods of psychosis.^{6,9,12,14}

Medication adherence in patients with schizophrenia is influenced by a multitude of factors. Existing research generally agrees that patients, social environment, and other treatment-related factors exert the most significant effect on medication adherence.^{5,12} Treatment-related factors encompass the complexity of the treatment regimen and medication side effects.^{8,15–17} Patient factors include insight, cognitive dysfunction, disease-related stigma, and depression.^{6,7,15,18,19} Regarding social environmental factors, social support is considered as a crucial factor.^{5,20} Social support encompasses a range of free assistance and help from social networks, spanning physical and emotional support.²¹ Given that a significant portion of individuals with schizophrenia reside in the community, supportive community and family environments are crucial for these patients.^{5,22} Therefore, social support is pivotal for patients with schizophrenia and has been a focal point in various studies.^{23,24}

The impact of psychological distress on medical well-being has long been established.²⁵ This is also supported from a neurobiological perspective. Abnormalities in brain structures or neurotransmitter systems, such as the amygdala, hippocampus, and prefrontal cortex, may play an important role in the influence of psychological factors on the symptoms and management of mental disorders.^{26–29} A meta-analysis suggests that depression is associated with poor medication adherence across various chronic diseases.^{13,19} In patients with schizophrenia, improvements in depressive symptoms have been shown to correlate with good medication adherence.³⁰ This association may stem from the fact that patients with schizophrenia experiencing depressive symptoms encounter more challenges in doctor-patient communication, exhibit lower treatment satisfaction, lack motivation, social withdrawal, and a sense of hopelessness, resulting in non-adherence to medication.^{19,31,32} Due to societal misunderstanding, discrimination, and exclusion, the stigma of mental illness is a widespread and persistent issue globally.³³ Previous research has shown that stigma can lead to a variety of negative physical and mental outcomes for people with schizophrenia, including increased psychotic and depressive symptoms and poor medication adherence.^{34–36}

The existing research models have shown that in addition to directly affecting individual health behaviors, social support can foster healthy behaviors by influencing psychological processes, including decreasing stress appraisals, enhancing self-esteem, and reducing negative emotional states.^{37,38} In buffering theory, stigma is conceptualized as a stressor and it is posited that social support can mitigate its adverse effects, ultimately improving patients' depressive symptoms and medication adherence.^{33,39,40} Moreover, stigma and depression are often included in existing studies as mediating factors. For instance, an investigation involving HIV patients demonstrated that stigma acted as a mediator in the connection between social support and depression.⁴¹ Similarly, a study of Chinese tuberculosis patients showed that depression played a mediating role in the correlation between stigma and medication adherence.⁴² Additionally, research indicated that if people living with HIV have multiple sources of social support in times of need, it could reduce the levels of stigma, diminish depressive symptoms, and enhance adherence.⁴³ However, there is scarce research exploring the mechanisms by which stigma and depression mediate the role of social support in medication adherence among patients with schizophrenia.

This study aims to explore the serial mediating effect of stigma and depression on the association between social support and medication adherence. Based on previous findings regarding the impact of stigma on depressive symptoms and the serial mediating role of stigma and depression in HIV patients,^{33,43} we opted for the serial multiple mediation model. This model is designed to examine the serial mediation effects of stigma and depression, with the initial mediator being stigma and the subsequent mediator being depression. In this study, we postulated that the influence of social support on medication adherence is channeled through three pivotal pathways: (1) stigma mediates the association between social support and medication adherence; (2) depression mediates the association between social support and medication adherence; (3) stigma and depression serially mediate the association between social support and medication adherence.

Materials and Methods

Participants

This cross-sectional study was carried out in Changning District, Shanghai, China, from August to December 2023. There are approximately more than 3000 schizophrenia patients in Changning District who are managed by the Shanghai Changning Mental Health Center. Empirical power tables was used to estimate sample size, and the results showed that for a mediation power of 0.8, a minimum of 268 samples were required to conduct the bias-corrected bootstrap test.⁴⁴ The inclusion criteria were as follows: 1) age ranging from 18 to 65 years; 2) demonstrated a stable clinical condition, as assessed by a psychiatrist, with no alterations in medication within the three months preceding the assessment; 3) diagnosed with schizophrenia in accordance with the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; 4) possessed the capability to independently complete questionnaires or do so with assistance from investigators. Exclusion criteria include: 1) any history of brain trauma; 2) displayed symptoms of alcohol or substance abuse. There are 9 streets under the jurisdiction of Changning District. According to the sample size requirements, 35 stabilized patients with schizophrenia who meet the inclusion and exclusion criteria were recruited from each street through convenience sampling and were investigated by trained investigators and qualified psychiatrists. Finally, 302 valid questionnaires were recovered, with a valid rate of 95.87%. This study complied with the Declaration of Helsinki, and ethical approval was obtained from the Medical Research Ethics Committee of the School of Public Health, Fudan University (The international registry no. IRB00002408 and FWA00002399). Written informed consent was obtained before participation in the study.

Measurement

The researchers used the questionnaire that consisted of five parts: social support, stigma, depression, medication adherence, and demographic characteristics.

Demographic Characteristics

Demographic characteristics data included age, sex, body mass index (BMI), marital status, education level, employment status, and personal monthly income were collected.

Social Support

Social support across three dimensions (family, friends, and significant others) was measured using the Multidimensional Scale of Perceived Social Support (MSPSS).⁴⁵ Participants rated each item on a 7-point scale from 1 (very strongly disagree) to 7 (very strongly agree). The total score was calculated by summing the scores across all 12 items and then dividing by 12, maintaining a 1–7 scoring range. A higher mean score reflected a higher level of social support. In our study, Cronbach's alpha of the MSPSS Chinese version was 0.95.

Stigma

The perceived level of stigma was measured using the Stigma Scale for Chronic Illness 8-item version (SSCI-8).⁴⁶ The SSCI-8 consists of 8 items scored on a 5-point Likert scale ranging from 1 to 5. The total score was calculated by summing the scores across all 8 items and then dividing by 8, maintaining a 1–5 scoring range. Higher scores indicated higher levels of stigma. In the present study, Cronbach's alpha of the SSCI-8 Chinese version was 0.94.

Depression

The depression subscale of the Hospital Anxiety and Depression Scale (HADS-D) was used to assess depressive symptoms.⁴⁷ Participants rated 7 items on a 4-point Likert scale from 0 to 3. The total score ranges from 0 to 21, with higher scores signifying greater depression. Previous studies have demonstrated the reliability of this scale for use in patients with schizophrenia.^{48,49} In this study, Cronbach's alpha was 0.84.

Medication Adherence

The participants' medication adherence was assessed using the Medication Adherence Rating Scale (MARS), a self-report instrument consisting of 10 items.⁵⁰ Each item has two answers: yes/no. For item 1–6 and 9–10, the answer “no”

was scored as 1 point and the answer “yes” was scored as 0 point. For item 7 and 8, the answer “yes” was scored as 1 point and the answer “no” was scored as 0 point. The Total score ranged from 0 to 10, with higher scores reflecting better medication adherence. The MARS has been validated as an effective and reliable tool for patients with schizophrenia.^{51–53} In the present study, Cronbach’s alpha of the MARS Chinese version was 0.79.

Statistical Analysis

Statistical analysis was performed in R 4.3.2 (<http://www.R-project.org>). We presented the demographic characteristics of the samples and provided an overview of the distribution of medication adherence using descriptive statistics, independent-samples *T*-test, and ANOVA. Pearson correlation analysis was employed to assess the relationships among social support, stigma, depression and medication adherence. The serial multiple mediation effect was identified using the bootstrap analysis (bias-corrected CIs based on 5000 resamples). The mediating effect was considered statistically significant when the 95% CI did not include zero. The direct, indirect, and total effects were computed in the presence of a mediation effect. Additionally, age, sex, BMI, marital status, education level, employment status and personal monthly income were considered as covariates in the analysis.

Results

Preliminary Analyses

The final analysis included 302 patients with schizophrenia, and the demographic characteristics and distribution of medication adherence are presented in Table 1. The mean age of participants was 47.71 years (SD = 9.87), with

Table 1 Characteristics of the Participants by Medication Adherence

Characteristics	N (%)	Medication Adherence Mean ± SD	t/F	P
Age (years)			1.35	0.262
≤45	129 (42.72%)	6.78 ± 2.38		
46–55	93 (30.79%)	6.25 ± 2.54		
≥56	80 (26.49%)	6.49 ± 2.20		
Sex			−0.60	0.549
Male	139 (46.03%)	6.45 ± 2.58		
Female	163 (53.97%)	6.61 ± 2.22		
BMI (kg/m ²)			0.12	0.947
Underweight (<18.5)	8 (2.65%)	6.62 ± 2.88		
Normal weight (18.5–24.9)	166 (54.97%)	6.57 ± 2.39		
Overweight (25.0–29.9)	104 (34.44%)	6.43 ± 2.46		
Obese (≥30)	24 (7.95%)	6.71 ± 1.97		
Marital status			0.31	0.760
Married	67 (22.19%)	6.61 ± 2.25		
Unmarried/widowed/divorced	235 (77.81%)	6.51 ± 2.43		
Education level			0.01	0.978
<High school	84 (27.81%)	6.61 ± 2.37		
High school	130 (43.05%)	6.44 ± 2.44		
>High school	88 (29.14%)	6.61 ± 2.35		
Employment status			1.15	0.318
Employed	34 (11.26%)	7.12 ± 1.90		
Unemployed	206 (68.21%)	6.48 ± 2.49		
Retired	62 (20.53%)	6.42 ± 2.26		
Personal monthly income (CNY¥)			1.31	0.254
≤2000	78 (25.83%)	6.69 ± 2.30		
2001–3000	112 (37.09%)	6.65 ± 2.29		
≥3001	112 (37.09%)	6.31 ± 2.55		

Abbreviations: N, number; SD, standard deviation.

Table 2 Pearson's Correlation Between Different Variables

	Social Support	Stigma	Depression	Medication Adherence
Social support	1.00			
Stigma	-0.31***	1.00		
Depression	-0.52***	0.47***	1.00	
Medication adherence	0.39***	-0.31***	-0.37***	1.00
Cronbach's Alpha	0.95	0.94	0.84	0.79
Mean \pm SD	4.87 \pm 1.01	2.33 \pm 0.78	6.68 \pm 4.17	6.54 \pm 2.39

Note: *** $P < 0.001$.

Abbreviation: SD, standard deviation.

a majority being female (53.97%). More than half of the patients with schizophrenia maintained a normal BMI (54.97%), and over two-thirds had attained at least a high school degree (72.19%). Marriage was reported by a minority of participants (22.19%), and a smaller proportion were currently employed (11.26%).

Correlation Analysis Among Study Variables

Table 2 displayed the mean scores and correlation coefficients for the study variables. The results showed that the mean scores for social support were 4.87 (SD = 1.01), for stigma were 2.33 (SD = 0.78), for depression were 6.68 (SD = 4.17), for medication adherence were 6.54 (SD = 2.39). Strong Cronbach's Alpha values were observed for social support (0.95), stigma (0.94), depression (0.84), and medication adherence (0.79). Medication adherence showed significant correlations with social support ($r = 0.39$), stigma ($r = -0.31$) and depression ($r = -0.37$). Social support revealed significant correlations with stigma ($r = -0.31$) and depression ($r = -0.52$). Stigma exhibited a significant correlation with depression ($r = 0.47$).

Mediation Analyses

Figure 1 and Table 3 presented serial multiple mediation analysis results. As anticipated, there was a direct and significantly positive association between social support and medication adherence ($\beta = 0.69$, $p < 0.001$). Elevated levels of social support correlated with reduced levels of stigma ($\beta = -0.23$, $p < 0.001$) and depression ($\beta = -1.72$, $p < 0.001$). Increased levels of stigma were linked to an increase in levels of depression ($\beta = 1.83$, $p < 0.001$). Moreover, heightened levels of stigma ($\beta = -0.45$, $p = 0.013$) and increased levels of depression ($\beta = -0.09$, $p = 0.017$) were both associated with a decline in medication adherence.

Bootstrapping analysis revealed that the association between social support and medication adherence operated indirectly through stigma ($\beta = 0.11$, 95% CI: 0.03, 0.18). Additionally, social support was indirectly associated with medication adherence through depression ($\beta = 0.15$, 95% CI: 0.04, 0.30). Further analysis indicated that social support had an indirect association with medication adherence through both stigma and depression ($\beta = 0.04$, 95% CI: 0.01, 0.07).

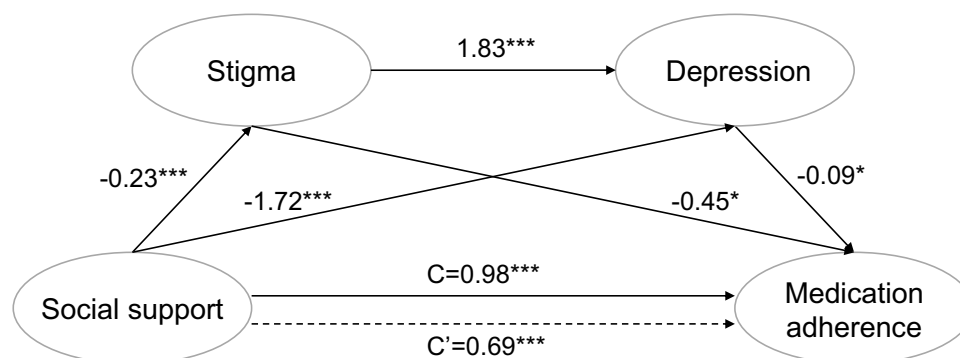


Figure 1 The serial multiple mediation role of stigma and depression on the association between social support and medication adherence with regression coefficients. C total effect; C' direct effect. * $p < 0.05$, *** $p < 0.001$.

Table 3 Bootstrap Analysis^a of Total, Direct, Indirect Effects of Social Support on Medication Adherence Through Stigma and Depression

Paths	β	SE	95% CI	P
Direct effect				
Social support → medication adherence	0.69	0.16	(0.38, 1.09)	<0.001
Indirect effect				
Total indirect effect	0.30	0.09	(0.14, 0.46)	<0.001
Social support → stigma → medication adherence	0.11	0.04	(0.03, 0.18)	0.010
Social support → depression → medication adherence	0.15	0.07	(0.04, 0.30)	0.033
Social support → stigma → depression → medication adherence	0.04	0.02	(0.01, 0.07)	0.031
Total effect	0.98	0.17	(0.66, 1.32)	<0.001

Notes: ^aNumber of bootstrap samples: 5000. Age, sex, BMI, marital status, education level, employment status and personal monthly income were controlled in the analysis.

Discussion

The current study offered evidence of an association between social support and medication adherence. The findings indicated that stigma and depression could separately mediate the relationship between social support and medication adherence. Furthermore, there is a serial mediating effect of stigma and depression on the association between social support and medication adherence.

Medication adherence is crucial for stabilizing schizophrenia, yet the medication adherence score in this study sample (6.68) was lower compared to a study of schizophrenia patients in Nigeria (7.09).⁵² This underscores the necessity of implementing targeted measures to enhance medication adherence among schizophrenia patients in this region, such as psychosocial intervention and the establishment of a supportive social environment. This study found a strong positive relationship between social support and medication adherence. Social support is an important contributor to personal health and well-being.³⁸ Diverse sources of social support from clinical mental health workers, community staff, and families can significantly enhance patient medication adherence, thereby maintaining symptom stability.⁵⁴ Furthermore, environmental support strategies that incorporate medications into daily routine, such as phone reminders and the use of unit medication packaging, proves instrumental in enhancing patient medication adherence.^{10,55,56}

Consistent with other studies, stigma and depression levels were significantly negatively correlated with medication adherence in patients with schizophrenia.^{30,34,57} The negative impact of depression on medication adherence may be diverse, encompassing factors such as decreased patient energy, increased feelings of despair, and heightened barriers to doctor-patient communication.^{19,31} The emergence of depressive symptoms in patients could be a reaction to adverse life events, such as social discrimination, rejection, and the impact of negative psychological stressors like stigma.^{42,58} These adverse psychological factors further contribute to social withdrawal in patients, consequently leading to a decline in medication adherence.

In this study, patients' increased levels of social support could reduce the levels of stigma and further enhance medication adherence. Numerous studies have demonstrated that social support, whether from family, friends, or significant others, contributes to the reduction of stigma.^{33,39} Furthermore, the perception of high levels of social support is associated with a decrease in disease-related stigma, resulting in confidence and perseverance in treatment, and further contributing to improved medication adherence.⁵⁹ In addition, we also found that an increase in levels of social support was associated with a reduction in levels of depression, further enhancing medication adherence. Similarly, support from various sources is considered to have independent protective effects against depression.⁶⁰ This may occur through the direct benefits of social relationships in safeguarding mental health or indirectly through buffering against stressful circumstances, such as reducing stigma.⁶⁰ Adequate social support can assist patients in overcoming negative psychological symptoms, leading to improved medication adherence.⁶¹

The findings demonstrated that strong social support could decrease the levels of stigma, followed by a reduction in depression levels, ultimately contributing to the enhancement of medication adherence. Therefore, if patients with schizophrenia receive adequate social support from various sources during treatment, it may diminish their perception

of disease-related stigma, reduce depressive symptoms, and result in better medication adherence. This finding is consistent with existing research, suggesting that healthcare providers should not only create supportive family and social environments but also place increased emphasis on psychological interventions for patients with schizophrenia.⁴³ This comprehensive approach can reduce the levels of stigma and depression among patients, ensuring the effectiveness of social support in promoting medication adherence.

This study had several limitations. First, self-report measures of medication adherence may be less accurate than electronic monitoring in patients with schizophrenia. But existing evidence also suggests that it is considered feasible to collect reliable data from people with schizophrenia through self-reporting.⁶² Second, the study sample was exclusively drawn from Shanghai, and a convenience sampling method was employed. Given potential regional cultural disparities, variations in social support, stigma, depression, and medication adherence among patients with schizophrenia may exist across different regions. This may introduce selection bias and limit the generalizability of the findings. Third, we solely computed Cronbach's Alpha value to assess the internal consistency of the scales. Nevertheless, given the absence of repeated measurements and the assessment of each questionnaire by a single investigator, inter-rater reliability and test-retest reliability were not calculated in this study, which may affect the further test of scale reliability. Lastly, the cross-sectional nature of this study warrants caution in interpreting causal relationships between variables. Nonetheless, the findings of this study offer preliminary insights and avenues for exploration in further longitudinal studies.

Conclusion

The findings highlight the role of stigma and depression as serial mediators of the relationship between social support and medication adherence. This serial multiple mediation model holds significant implications for the management of patients with schizophrenia. It underscores the importance of integrating social support interventions with psychological interventions aimed at reducing stigma and depression, thereby effectively enhancing medication adherence in patients with schizophrenia.

Data Sharing Statement

The datasets used to support the findings of this study are available from the corresponding author on reasonable request.

Ethics Approval and Informed Consent

This study was approved by the Medical Research Ethics Committee of the School of Public Health, Fudan University (The international registry no. IRB00002408 & FWA00002399).

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Disclosure

The authors report no conflicts of interest in this work.

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