ORIGINAL RESEARCH

The Relationship Between Intolerance of Uncertainty and Treatment Adherence: The Moderating Effect of Self-Compassion on the Chain Mediation Model

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Purpose: The low follow-up compliance of young and middle-aged patients with newly diagnosed pulmonary nodules warrants attention, primarily due to a series of factors such as occupational, familial, and social pressures. Enhancing follow-up adherence is essential for preventing pulmonary nodule progression and reducing lung cancer mortality. Existing research indicates that intolerance of uncertainty is closely associated with patients' follow-up compliance; however, further in-depth investigation into its influencing mechanisms and potential improvement strategies is required.

Patients and Methods: This study conducted a questionnaire survey among 319 young and middle-aged patients newly diagnosed with pulmonary nodules, examining the moderating effect of self-compassion on follow-up compliance and investigating the chain intermediary role of negative interpretation bias and trust in linking intolerance of uncertainty to follow-up compliance.

Results: The study found that women, urban residents, and patients over 50 years old demonstrated relatively higher follow-up compliance. Intolerance of uncertainty was found to negatively predict follow-up compliance and indirectly influenced patients' follow-up behavior through the mediating effects of negative interpretation bias and trust. Furthermore, self-compassion significantly moderated the relationship between trust and follow-up compliance.

Conclusion: The findings provide a solid theoretical foundation for developing multidimensional interventions targeting both protective and risk factors. Specifically, mitigating the impact of intolerance of uncertainty on follow-up compliance can improve long-term patient health outcomes. The novel application of the chain mediation model provides valuable insights for future research and clinical practice, particularly in enhancing patient engagement and adherence to follow-up care. Future longitudinal studies are needed to explore additional influencing factors and validate these findings.

Keywords: IU, interpretation bias, trust, self-compassion, initial diagnosis of pulmonary nodules, compliance

Introduction

Pulmonary nodules are small lung tissues with a diameter of no more than 3 cm, which can be benign or malignant.¹ With the advancement of CT technology, the detection rate of pulmonary nodules has increased significantly. A study involving 53,202 individuals undergoing physical examinations in China found a detection rate as high as 67.31%, reaching 81.23% among those aged over 55 years.² While most pulmonary nodules are benign, 2–3.6% may develop into lung cancer, and a considerable proportion are classified as "lung nodules of uncertain nature".¹ Consequently, standardized follow-up is crucial. The 2011 National Lung Screening Trial (NLST) in the United States confirmed that low-dose spiral CT (LDCT) screening can reduce lung cancer mortality in high-risk populations by 20%.³ Based on this

699

evidence, current lung cancer screening guidelines, both domestically and internationally, recommend LDCT screening for high-risk populations.^{4,5} The Chinese guidelines even suggest universal screening for individuals aged 45 and older, with close monitoring of nodule changes to enhance early detection rates and improve disease prognosis.¹ Follow-up usually lasts from 2 to 5 years, with examination frequency (ranging from 2 to 5 times) determined by the patient's risk factors, nodule size, and morphology. Patients lacking regular follow-up are more likely to experience worsening pulmonary nodules due to delayed detection, or even progression to lung cancer, thereby increasing health risks.¹

However, due to the uncertainty of the disease and repeated examinations, young and middle-aged patients often experience significant psychological pressure, making them prone to anxiety, depression, and other negative emotions, which in turn affects follow-up adherence. Therefore, improving the follow-up adherence of young and middle-aged patients may be crucial for the early detection and prevention of lung cancer.⁶

Intolerance of Uncertainty and Treatment Adherence to Follow-up

The notion of intolerance of uncertainty (IU) originated within the explanatory framework for the development of anxiety disorders. Krohne claimed that cognitive intolerance of uncertainty in life and physiological intolerance of emotional arousal are the primary contributors to the development of anxiety disorders; however, he did not provide a definitive explanation of intolerance of uncertainty (IU).⁷ After that, Dugas posited that an individual's excessive or uncontrolled anxiety response when facing uncertain situations, leading to strong and persistent avoidance and resistance to uncertainty in 1997.⁸ The prevalent instruments for assessing intolerance of uncertainty are the Intolerance of Uncertainty Scale (IUS), the Intolerance of Uncertainty Scale-12 (IUS-12), and the Intolerance of Uncertainty Inventory (IUI).⁹

Existing studies have shown that there is a correlation between IU and treatment adherence to follow-up, but the research results show certain complexity and inconsistency.⁹ On the one hand, studies have shown that high levels of IU are generally associated with lower treatment adherence to follow-up,¹⁰ especially in cancer patients and patients with chronic diseases. IU often leads to poor coping strategies such as cognitive avoidance, thereby reducing patients' treatment adherence to follow-up. However, on the other hand, some studies have found that in specific situations, IU may inspire patients to take positive management behaviors.¹¹ For example, in HIV-positive individuals, higher tolerance for ambiguity is associated with higher treatment adherence to follow-up. This diversity of research results shows that the effect of IU on treatment adherence to follow-up is not single or linear, and may be regulated and mediated by multiple factors.^{12–16} In recent years, Langerian mindfulness has been proposed as a potential regulatory mechanism to help individuals adapt to uncertainty and alleviate anxiety and avoidance behavior, given its emphasis on cognitive reconstruction and has a relatively limited influence on internal emotional regulation. Its effectiveness in medical decision-making may vary based on individual psychological traits. Therefore, exploring the mechanistic link between IU and treatment adherence, as well as identifying other potential regulatory factors, is crucial for a deeper understanding of this complex relationship.

Potential Mediating and Chain Mediating Role of Negative Interpretation Bias and Trust

The extent to which patients interpret information negatively has been extensively studied as one of the many factors that influence compliance with treatment adherence to follow-up. Negative interpretation bias is the inclination of patients to perceive neutral or ambiguous information as negative or threatening.^{15,16} Research demonstrates that as patients' intolerance for uncertainty (IU) increases, so does their negative interpretation bias.¹⁹ This increases the likelihood of disregarding or misinterpreting medical advice, resulting in decreased adherence to follow-up instructions.^{20,21} In other words, when patients face an uncertain medical environment, negative interpretation bias significantly influences their emotional and behavioral responses. According to the conservation of resources theory,²² when individuals perceive a threat, they tend to protect their psychological resources, such as emotional stability or cognitive ability. This mechanism may cause them to interpret information more negatively to quickly react to potential dangers. Though initially beneficial, this approach may ultimately exacerbate negative interpretation bias, reducing treatment adherence to

follow-up and health outcomes.^{23–25} Specifically, patients newly diagnosed with lung nodules are particularly susceptible to this cognitive pattern. Over time, this buildup of negative emotions may lead to follow-up discontinuation or delays in seeking medical care, ultimately worsening disease progression and quality of life.^{19,26–28}

Physician trust is not only patients' trust in Medical stuffs' professional abilities and professional ethics, but more importantly, it stems from patients' expectations for treatment effects and their need for a sense of security during the treatment process.²⁹ When patients are in a highly uncertain medical environment, such as when faced with unclear disease diagnosis or treatment effects, their fear and anxiety about the future are often heightened. In this case, physician trust becomes a key factor in whether the patient is willing to accept and continue treatment.^{29–32}At the same time, as patients' intolerance of uncertainty (IU) increases, their tolerance for the unknown decreases significantly, making them more sensitive to any unclear or ambiguous information during treatment.²⁹ If the physician fails to promptly and effectively explain the specific details and expected effects of the treatment plan, the patient's trust is likely to decline rapidly. As a result, patients may begin to doubt medical advice and be reluctant to follow it,^{29,31,33} such as not taking medications on time or missing important treatments and tests. In addition, once a crisis of trust occurs, it will not only affect patients' compliance, but may also cause them to become more psychologically and emotionally unstable This instability often worsens their anxiety and depression, further diminishing the effectiveness of treatment. Therefore, establishing and maintaining a trusting relationship between doctors and patients is particularly important to ensure the smooth implementation of the treatment plan and ultimately improve the treatment effect.³⁴

Research indicates that negative interpretation bias markedly intensifies health anxiety by amplifying health concerns and diminishing trust in healthcare practitioners.^{21,35} Patients who interpret ambiguous information adversely exhibit greater difficulties in believing medical advice, which subsequently impacts treatment compliance.^{36–38} Moreover, the correlation between interpretation bias and trust in influencing treatment adherence is well-documented. Interpretation bias serves as a critical predictor of how patients understand medical information. Studies demonstrate that when patients exhibit a high negative interpretation bias while interpreting medical orders and treatment recommendations, they tend to reduce their trust in medical staff, leading to increased negative emotions. This bias not only weakens their understanding and acceptance of treatment plans but may further reduce treatment adherence through diminished trust.^{37,38} Within the framework of social cognitive theory,^{39,40} interpretation bias, as a key social cognitive factor, profoundly impacts how patients interpret medical instructions and treatment recommendations.^{41–43} When patients perceive information negatively, they are less likely to expect that following medical orders will result in positive health outcomes, and thus, they may become less willing to adhere to these orders. This negative expectation undermines their trust in medical staff, making them more likely to respond to uncertainty with negativity, thereby exacerbating negative emotions. Based on this analysis and in conjunction with Hypothesis 2 and Hypothesis 3, it is suggested that interpretation bias and trust may serve as mediating factors between intolerance of uncertainty and treatment adherence in patients with first-time pulmonary nodules, with a significant correlation potentially existing between these two variables.

Self-Compassion as a Moderator

However, as we previously mentioned, not all patients with high intolerance of uncertainty (IU) will experience decreased treatment adherence. Studies have shown that engaging in self-compassion has a significant positive moderating effect on patients' interpretation bias and trust.^{44–46} Self-compassion is the practice of treating oneself with kindness, understanding, and support in times of suffering or failure, rather than being overly critical or harsh. It comprises three dimensions: self-kindness (being caring toward oneself), common humanity (recognizing that suffering is a shared human experience), and mindfulness (maintaining a balanced awareness of one's emotions without over-identifying with them). For example, the dimension of mindfulness helps patients manage negative emotions more objectively, thereby reducing misunderstandings about treatment plans.⁴⁷ Similarly, the dimension of self-kindness aids patients in facing treatment with a more positive attitude, thus enhancing their trust in medical staff.⁴⁸ However, it should be noted that not all dimensions of self-compassion have a positive impact on patients. For example, over-identification with this negative dimension may cause patients to become more obsessed with negative emotions, find it difficult to look at their situation objectively, and ultimately doubt the advice of medical staff, even weakening their trust in the medical team.^{49,50}

Therefore, in clinical practice, medical staff should pay attention to the balance of patients' self-compassion to avoid the potential weakening effect of over-identification on patients' trust.

Hypotheses

On this basis, this study took patients with pulmonary nodules diagnosed for the first time as the research subjects. By constructing a moderated chain mediation model, it explored the impact of intolerance of uncertainty on treatment adherence to follow-up, examined the mediating roles of interpretation bias and caregiver-patient trust in the model, and analyzed the moderating effect of self-compassion on treatment adherence to follow-up. This study provides relevant research support for improving patients' treatment adherence to follow-up and proposes the following hypotheses:

H1: IU significantly and positively predicts a reduction in treatment adherence to follow-up.

- H2: Negative interpretation bias mediates the relationship between IU and treatment adherence to follow-up.
- H3: Patients' trust is another mediating variable between IU and treatment adherence to follow-up.
- H4: Negative interpretation bias and trust serve as sequential mediators that link IU with treatment adherence to follow-up.
- H5: Self-compassion moderates the effect of negative interpretation bias on treatment adherence to follow-up within the chain mediation model.
- **H6**: Self-compassion moderates the effect of caregiver-patient trust on treatment adherence to follow-up within the chain mediation model.

The theoretical model is shown in Figure 1.

Methods

This study was conducted at a tertiary hospital in Henan Province from November 2022 to August 2024. Participants were recruited from the respiratory outpatient department of the hospital. Data collection was conducted using a mobile phone-based QR code for participants to complete the questionnaires. All data collectors underwent standardized training, where they explained the study's purpose and instructions for completing the questionnaires to the patients, ensuring they filled out the forms accurately and in accordance with the prescribed guidelines. Investigators were available to provide immediate assistance and address any questions patients had during the completion process, ensuring that the questionnaires were filled out properly.



Figure I The Proposed Moderated Mediation Model.

Participants and Procedure

To determine the appropriate sample size, we used G*Power 3.1 software to perform a priori power analysis. Based on the requirements for multiple factor analysis and a medium effect size of $f^2 = 0.15$, two-tailed $\alpha = 0.05$, the minimum sample size required was 183 participants. To account for a 10% rate of invalid responses, the final sample size was adjusted to 202 participants. In this study, a total of 319 patients with newly diagnosed lung nodules were identified through convenience sampling. Invalid samples included participants with identical responses across multiple items and those with missing data. After excluding these invalid samples, 308 valid data points remained, resulting in an inclusion rate of 96.55%.

The final valid sample consisted of patients aged 41 to 60 years, including 149 males (48.38%) and 159 females (51.62%). For educational attainment, 65 patients (21.10%) had completed junior high school or less, 67 (21.75%) had finished high school or technical secondary education, and 176 (57.14%) held a college degree or higher. With respect to per capital monthly income, 104 patients (33.77%) earned less than 5000 yuan, 140 (45.45%) earned between 5000 and 10,000 yuan, and 64 (20.78%) earned more than 10,000 yuan. Regarding residential location, 105 patients (11.36%) lived in urban areas, while 203 (61.58%) resided in rural areas.

Measures

Intolerance of Uncertainty

In 2013, Carleton revised the Uncertainty Intolerance Scale (IUS-12),⁵¹ which was later translated into Chinese by Zhang Yajuan in 2017,⁵² followed by reliability and validity testing. The scale consists of 12 items, divided into two dimensions: anticipatory anxiety (7 items) and inhibitory anxiety (5 items). It employs a Likert 5-level scale and does not include reverse scoring. Higher scores indicate a greater level of IU. The Chinese version of IUS-12 has a Cronbach's α coefficient of 0.878, and confirmatory factor analysis results are $\chi^2/df \approx 3832.673/66 \approx 58.071$, TLI = 0.908, CFI = 0.926, and RMSEA = 0.001.

Interpretation Bias

The Interpretation Questionnaire (IQ), developed by Beard and Amir in 2010, consists of 22 ambiguous situations.⁵³ Three types of interpretations accompany each story: negative interpretation, neutral interpretation, and positive interpretation, evaluated using a 5-point Likert scale. The participants' task is to evaluate the likelihood of each interpretation separately. The negative interpretation sub-scale demonstrated a Cronbach's α coefficient of 0.899. This study focused solely on negative interpretation bias due to its pivotal role in cognitive bias theory and its influence on how individuals process uncertain information. Patients often question medical recommendations because of negative interpretation bias, which then impacts treatment adherence to follow-up. By concentrating on negative interpretation bias, the study more clearly highlights its unique effect on patient adherence.

Trust

The Chinese revised and adapted version of the Wake Forest Physician Trust Scale (WFPTS) was developed by Dong Enhong and Bao Yong.⁵⁴ It has 10 items and is divided into two dimensions: Benevolence and Technical Competence. The scale is scored on a Likert-5 scale, where 1 means "strongly disagree" and 5 means "strongly agree". The higher the score, the higher the patient's trust in the physician. The overall Cronbach's α coefficient of the scale was 0.89, indicating good internal consistency. The results of confirmatory factor analysis showed that χ^2 /df was 1.49, TLI was 0.93, CFI was 0.97, RMSEA was 0.07, and SRMR was 0.07, indicating that the scale had good structural validity.

Treatment Adherence to Follow-up

The General Adherence Scale (GAS), developed by DiMatteo and Hays,⁵⁵ consists of 5 items and is a unidimensional scale designed to assess patients' overall compliance with physician recommendations. It utilizes a Likert-6-point scoring system, where the first and third items are reverse-scored, while the remaining items are forward-scored. Higher scores indicate better adherence. In this study, the Cronbach's α coefficient for the scale was 0.942, demonstrating strong internal consistency. Confirmatory factor analysis results showed that $\chi^2/df = 2.032$, TLI = 0.992, CFI = 0.996, RMSEA = 0.072, and SRMR = 0.011, indicating that the scale has excellent model fit and structural validity.

Self-Compassion

The Self-Compassion Scale (SCS) was compiled by Neff.⁵⁶ It consists of 26 items, divided into 6 dimensions: Self-Kindness, Self-Judgment, Common Humanity, Isolation, Mindfulness, and Over-identified. The scale uses a Likert 5-point scale, with some items rated in the opposite direction. A higher score indicates a higher level of self-compassion. In this study, the Cronbach's α coefficient of the Chinese version of the SCS was 0.84, indicating good internal consistency. Confirmatory factor analysis results were $\chi^2/df = 1.49$, TLI = 0.93, CFI = 0.97, RMSEA = 0.07, and SRMR = 0.07, demonstrating good structural validity.

Control Variables Selection

In this study, gender, age, and residence were selected as control variables due to their significant effects on treatment adherence, as indicated by preliminary statistical analyses (independent sample t-tests and one-way ANOVA). These results align with previous research, which has shown that men tend to exhibit different adherence rates than women,⁵⁷ younger patients generally have higher adherence,⁵⁸ and urban residents typically show better adherence than those living in rural areas. Thus, these variables were included to account for their potential impact on treatment adherence outcomes.^{57,58}

Statistical Analyses

The analysis was performed using SPSS 26.0 statistical software, incorporating the PROCESS macro and Amos 23.0, both developed by Hayes. These tools were employed for assessing reliability and validity, conducting descriptive statistics, correlation analysis, regression analysis, and evaluating moderated effects through chain mediation analysis. To test the chain mediation effect, the nonparametric percentile bootstrap method was applied. Specifically, the PROCESS macro (Model 7) was used to examine the mediating roles of interpretation bias and physician trust in the relationship between intolerance of uncertainty (IU) and treatment adherence to follow-up.

Results

Common Method Deviation Test

Given that the data in this study were obtained solely from patient self-reports, standard bias testing methods were applied. The data were analyzed using unrotated principal component analysis in Harman's one-factor test, where the eigenvalue of the first factor was 17.589. A total of 30 factors had eigenvalues greater than $1,^{59}$ with the first factor explaining 14.781% of the variance, well below the 40% threshold. Thus, the study's data do not exhibit significant common methodological bias.

Analysis of the Overall Characteristics and Demographic Variability of Patients' Treatment Adherence to Follow-up

The average score of patients' treatment adherence to follow-up was 18.601, with a standard deviation of 6.997. Our study revealed a coefficient of variation of 37.619%, signifying considerable variability in compliance scores among patients, with some exhibiting markedly poorer compliance than the average. This disparity underscores the necessity of directing interventions towards low-adherence patients, as enhancing their compliance may potentially improve overall treatment outcomes. (For further details, please refer to the <u>Supplementary Table 1</u>).

This study utilized independent sample t-tests and one-way analysis of variance to examine differences in patient treatment adherence to follow-up across factors such as gender, age, marital status, residence, occupation type, education level, family income, medical expenses, religious beliefs, smoking, and lung cancer family history. The results demonstrated significant variations in patients' treatment adherence too follow-up in aspects gender, age group and residence.

Men exhibited lower adherence compared to women, urban residents showed greater adherence than their rural counterparts, and patients aged 41–45 and 46–50 years tend to exhibit markedly more adherence compared to those aged 51–55 and 56–60 years.

Relationship Between Intolerance of Uncertainty and Chain-Mediated Effect Test Patients' Treatment Adherence to Follow-up

This study investigated the impact of prospective anxiety and inhibitory anxiety related to IU on patients' treatment adherence to follow-up. (For further details, please refer to the <u>Supplementary Tables 2</u> and 3). The findings indicated that the level of prospective anxiety (2.805 ± 1.221) was somewhat lower than inhibitory anxiety (2.829 ± 1.237). There was a significant negative association between prospective anxiety and treatment adherence to follow-up (p = -0.414), and the association between inhibitory anxiety and treatment adherence to follow-up (p = -0.414), and the association between inhibitory anxiety and treatment adherence to follow-up (p = -0.398), as shown in Table 1.

This study aimed to investigate the extent to which patient IU affects treatment adherence to follow-up, under the premise that IU and its dimensions are significantly correlated with patient compliance. A linear regression analysis was conducted, using patient IU as the independent variable and demographic characteristics such as gender, place of residence, and age as control variables. These demographic variables were found to have significant differences in compliance. Even after accounting for gender, place of residence, and age, IU still had a strong negative impact on patient treatment adherence to follow-up. This effect was statistically significant ($\beta = 0.445$, t=-7.449, p=0.000<0.01). This demonstrates that while gender, place of residence, and age group are significantly correlated with treatment adherence to follow-up, IU has a distinct and independent effect. Table 2 demonstrates that for each additional standard unit of IU, there is a corresponding decrease of 0.445 in treatment adherence to follow-up, suggesting that patients with greater IU are more likely to have reduced adherence to treatment.

Chain-Mediated Effect Test

First, interpretation bias and physician trust were related to IU and treatment adherence to follow-up. The results showed that there was a significant two-by-two correlation between IU, physician trust, interpretation bias, and treatment adherence to follow-up. More specifically, IU was significantly positively correlated with negative interpretation bias, while negatively correlated with physician trust and treatment adherence to follow-up. Interpretation bias was

Table I Means, Standard Deviations, and Correl	lations of the Variables in This Study ($N = 308$)
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	M (SD)	Treatment Adherence to Follow-up	Intolerance of Uncertainty	Prospective Anxiety	Inhibitory Anxiety
Treatment adherence to follow-up	3.720±1.399	I			
Intolerance of uncertainty	2.815±1.172	-0.427**	I		
Prospective anxiety	2.805±1.221	-0.414**	0.967**	I	
Inhibitory anxiety	2.829±1.237	-0.398**	0.936**	0.816**	ļ

Note: **p<0.01.

Model	В	SE	Beta	t	Þ	VIF				
Common Element	3.629	0.598	-	6.074	0.000**	-				
Independent variable Control variable	IU Gender Age group	-0.445 0.586 0.146	0.06 0.138 0.061	-0.373 0.21 0.119	-7.449 4.241 2.396	0.000** 0.000** 0.017*	1.038 1.014 1.025			
R ² F	Residence	-0.524	0.524 0.169 -0.154 -3.105 0.002** 1.017 0.269 F (4303)=27.940, p=0.000							
Dependent variable =	Treatment ad	herence t	o follow-	up						

Table 2 Results of Regression Analysis of IU and Treatment Adherence

Note: *p<0.05 **p<0.01.

Abbreviations: SE, standard error; VIF, variance inflation factor.

Variables	I	2	3	4
I. Treatment adherence to follow-up	I			
2. Intolerance of uncertainty	-0.427**	I.		
3. Negative interpretation bias	-0.268**	0.17 9 **	I.	
4. Trust	0.388**	-0.173**	-0.165**	Ι

 Table 3 Correlations of All Variables in This Study (N = 308)

Notes: *p<0.05 **p<0.01.

 Table 4 Regression Analysis of the Relationship of Variables in the Intermediary Model

	Negative Interpretation Bias						Trust			Treatment Adherence to Follow-up					
	В	SE	t	Þ	β	В	SE	t	Þ	β	В	SE	t	Þ	β
Constant	2.298**	0.552	4.16	0	-	3.168**	0.593	5.344	0	-	3.184**	0.597	5.338	0	-
Gender	0.042	0.128	0.326	0.745	0.019	0.281*	0.133	2.109	0.036	0.118	0.507**	0.129	3.924	0	0.181
Age group	0.014	0.056	0.255	0.799	0.015	0.019	0.059	0.321	0.748	0.018	0.143*	0.057	2.537	0.012	0.117
Residence	0.133	0.156	0.854	0.394	0.049	-0.111	0.163	-0.681	0.497	-0.038	-0.456**	0.157	-2.908	0.004	-0.134
Intolerance of Uncertainty	0.171**	0.055	3.096	0.002	0.178	-0.131*	0.059	-2.24	0.026	-0.129	-0.362**	0.057	-6.369	0	-0.303
Negative Interpretation Bias						-0.147*	0.06	-2.444	0.015	-0.138	-0.198**	0.058	-3.392	0.001	-0.159
Trust											0.318**	0.055	5.739	0	0.27
R ²		•	0.035		•	0.064			•	0.375					
Adjusted R ²			0.022			0.049							0.363		
F		F (4303)	=2.731, p	=0.029			F (5302	2)=4.158, p	=0.001		F (6301)=30.104, p=0.000				

Notes: *p<0.05 **p<0.01.

significantly negatively correlated with physician trust and treatment adherence to follow-up. Physician trust was significantly positively correlated with treatment adherence to follow-up, as shown in Table 3.

The study findings demonstrated that negative interpretation bias and physician trust acted as sequential mediators in the relationship between IU and adherence to follow-up in patients. The overall effect of IU on treatment adherence to follow-up, as indicated by the mediation effect value of 0.362, accounted for 81.40% of the total effect. The results are presented in Table 4 and Figure 2.

Specifically, the mediation effect is composed of three indirect effect pathways: indirect effect 1 (0.042) through the pathway of "IU \rightarrow physician trust \rightarrow treatment adherence to follow-up"; indirect effect 2 (0.034) through the



Figure 2 Chain-mediated Effect of Interpretation Bias and Trust.

Table 5 Standardized Bootstrap Estimates and 95% Confidence Intervals for Indirect Effe

Model Pathway	Effect	BootLLCI	BootULCI	Relative Mediating Effect
Intolerance of Uncertainty⇒ Negative interpretation bias ⇒Treatment Adherence to Follow-up	-0.034	-0.057	-0.007	7.61%
Intolerance of uncertainty⇒Trust⇒Treatment adherence to follow-up	-0.042	-0.071	-0.004	9.36%
Intolerance of Uncertainty⇒ Negative interpretation bias ⇒Trust⇒Treatment adherence to follow-up	-0.008	-0.016	-0.001	1.80%

Notes: BootLLCI refers to the lower limit of the 95% confidence interval from Bootstrap sampling, BootULCI refers to the upper limit of the 95% confidence interval from Bootstrap sampling, bootstrap type: percentile bootstrap method.

pathway of "IU \rightarrow interpretation bias \rightarrow treatment adherence to follow-up"; and indirect effect 3 (0.008) through the pathway of "IU \rightarrow interpretation bias \rightarrow physician trust \rightarrow treatment adherence to follow-up". The proportions of these three paths in the total effect sizes were 9.43%, 7.64%, and 1.80%, respectively. These effect sizes, while small, have important clinical implications, particularly in improving patient adherence to follow-up care. For example, enhancing physician trust and addressing negative interpretation bias may lead to modest, but significant improvements in treatment adherence. The bootstrap 95% confidence interval of indirect effect 1, indirect effect 2 and indirect effect 3 did not include 0, meaning that all 3 paths were statistically significant. The results of the mediation effect decomposition are shown in Table 5.

Moderated Mediation Effect Test

This study employed the SPSS PROCESS plug-in model to examine the chain mediation effect and investigate the moderating role of self-compassion in the relationships among IU, interpretation bias, physician trust, and treatment adherence to follow-up. The findings indicated that in the chain mediation model incorporating self-compassion, the interaction between interpretation bias and self-compassion did not significantly influence patient compliance ($\beta = -0.014$, t = -0.272, P > 0.05). Conversely, the interaction between trust and self-compassion showed a significant positive effect on patient compliance ($\beta = 0.120$, t = 2.415, P < 0.05). This suggests that self-compassion moderates the relationship between trust and patient compliance, serving as a key factor in the sequence "IU \rightarrow interpretation bias \rightarrow trust \rightarrow patient compliance". The impact of physician trust on treatment adherence at varying self-compassion levels was further analyzed using simple slope analysis. When self-compassion was at an average level, physician trust significantly improved treatment adherence ($\beta = 0.389$, t = 6.353, p < 0.001, 95% CI [0.269, 0.509]); at high self-compassion levels (+1 SD), this positive effect was even stronger ($\beta = 0.535$, t = 6.392, p < 0.001, 95% CI [0.371, 0.699]); conversely, at low self-compassion levels (-1 SD), the positive effect, though weaker, remained significant ($\beta = 0.243$, t = 2.751, p = 0.006, 95% CI [0.070, 0.416]). These findings highlight that self-compassion, as a moderating variable, significantly enhances the association between physician trust and treatment adherence. Specifically, higher self-compassion levels amplify the positive impact of physician trust on adherence, whereas lower self-compassion levels attenuate this effect, though it remains present. Table 6 shows the overall moderating effect, and Table 7 presents results across different self-compassion levels.

Outcome Variable	Predictive Variable	R	R-squared	F	β	t
Treatment adherence to follow-up	-	0.562	0.316	23.184	-	-
	Intolerance of uncertainty	-	-	-	-0.427	-8.256
	Negative interpretation bias	-	-	-	-0.268	-4.868
	Trust	-	-	-	0.388	7.357
	Self-compassion	-	-	-	0.128	2.251
	Negative interpretation bias ×Self-compassion	-	-	-	-0.014	-0.272*
	Trust×Self-compassion	-	_	-	0.120	2.415

Table 6	Moderated	Mediation	Effect	Test
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Note: *p<0.05.

	Horizontal Value	Effect	SE	t	Þ	LLCI	ULCI
Low level of Self-compassion (-ISD)	2.217	-0.237	0.078	-3.04	0.003	-0.39	-0.084
Medium level of Self-compassion (-ISD)	3.279	-0.375	0.057	-6.624	0	-0.486	-0.264
High level of Self-compassion (+ISD)	4.342	-0.513	0.085	-6.032	0	-0.68	-0.347

 Table 7 Moderating Effects of Different Self-Compassion Levels

Note: LLCI refers to the lower limit of the 95% confidence interval, and ULCI refers to the upper limit of the 95% confidence interval.

Discussion

Differences in Treatment Adherence to Follow-up of Patients Across Demographic Characteristics

This study found that men had lower compliance than women, which is consistent with research conducted in the past 3–5 years. Literature indicates that women generally exhibit higher levels of anxiety and health awareness in managing their health, making them more likely to follow medical advice.⁶⁰ Although men may show higher compliance in some occupational or lifestyle-related diseases,⁶¹ overall, men's compliance in health management is generally lower than that of women, which may be related to men's avoidance of health issues and their insufficient awareness of associated risks. Furthermore, the result that patients under 50 years old have lower compliance than those over 50 is consistent with existing studies, which suggest that older patients are more focused on health management due to their heavier disease burden, which makes them more focused on health management.⁶² However, young people may exhibit higher compliance in some contexts, particularly with the help of technological interventions, such as mobile phone applications.⁶³ Lastly, urban patients have higher compliance than rural patients, which is related to the ease of access to medical resources and health knowledge.⁶⁴ However, improvements in adherence in rural areas may be linked to the strengthening of community support systems or policy reforms.^{65–67}

In summary, the results of this study are largely in line with research conducted in the past 3–5 years, with gender, age, and place of residence all significantly influencing compliance. Women, older patients, and urban residents show higher compliance, which aligns with differences in health awareness, disease burden, and access to medical resources. However, the inconsistent parts suggest that improving male compliance in particular disease contexts, the impact of technological interventions on younger demographics, and the potential for improving adherence through community support systems in rural areas all warrant further investigation. These differences highlight the need for targeted intervention strategies tailored to different groups.

IU as a Risk Factor for Decreased Treatment Adherence to Follow-up

The results of this study showed that IU had a significant negative predictive effect on treatment adherence to follow-up and was a risk factor for reduced patient follow-up adherence, which also echoed the results of existing studies.⁶⁸ One possible explanation is that IU is often accompanied by patients' interpretative bias in processing medical information, which may lead to patients' misunderstanding or rejection of follow-up medical orders, thereby affecting their compliance.⁶⁶ When patients face uncertain medical conditions, higher IU may exacerbate interpretative bias, which will further weaken the trust between patients and healthcare providers, thus reducing patients' confidence in and adherence to follow-up plans.^{66,69} Additionally, interpretative bias may make it difficult for patients to accurately process medical orders and recommendations, increasing antagonism during follow-up, and ultimately leading to a significant decrease in treatment adherence to follow-up.⁷⁰ From the perspective of healthcare providers, failure to promptly recognize and address patients' resistance to follow-up recommendations and reducing treatment effectiveness. On the other hand, patients with low treatment adherence to follow-up may attempt to alleviate the anxiety caused by IU through other means.⁷¹ Clearly, improving patients' self-compassion can mitigate the negative impact of IU on interpretative bias and patient-nurse trust. To a certain extent, self-compassion helps patients better manage their emotions and reduce negative interpretative bias, thereby enhancing the trust relationship between patients and healthcare

professionals. Ultimately, this improved trust and understanding will create a more favorable follow-up atmosphere for patients, increase treatment adherence to follow-up, and promote better long-term health outcomes.

Negative Interpretative Bias and Trust Also Deserve Attention

This study revealed that intolerance of uncertainty can affect patient compliance through negative interpretive bias and trust. Specifically, excessive intolerance of uncertainty in patients positively predicts negative interpretive bias, while negative interpretive bias in turn negatively predicts trust, which aligns with previous research findings.⁷² According to the Conservation of Resources Theory, when patients perceive uncertainty, their psychological resources—such as security, trust, and control over the future—are threatened. To safeguard these resources, patients tend to exhibit a negative interpretive bias, interpreting ambiguous or uncertain medical information as potential threats or adverse factors. This interpretive bias weakens trust in healthcare providers, leading to resistance or rejection of follow-up recommendations, thereby reducing adherence to follow-up care. In the face of uncertainty, patients are more inclined to protect their psychological resources than to follow medical advice, which directly impacts the implementation of follow-up care. Research shows that intolerance of uncertainty is indeed closely related to patients' negative interpretive bias, a relationship confirmed in numerous studies. For instance, Hall found that individuals with high intolerance of uncertainty are more likely to develop a negative interpretive bias when faced with ambiguous medical information, affecting their medical decisions.⁶⁶ This result supports the Conservation of Resources Theory, which asserts that individuals prioritize protecting their psychological resources when facing uncertainty, leading to heightened negative cognitive responses.

Building on this, Social Cognitive Theory further explains this mechanism. Once patients develop a negative interpretive bias, they are more likely to interpret medical advice and treatment recommendations as threatening or unfavorable. This leads to not only doubts about the medical information but also an exaggeration of perceived risks and an underestimation of treatment benefits. Social Cognitive Theory emphasizes the critical role of individual cognitive processes and personal beliefs in this dynamic. When patients' beliefs conflict with physicians' advice, they are more likely to rely on their cognitive biases, which further intensifies misinterpretations of the advice and weakens trust in physicians, ultimately significantly reducing treatment adherence to follow-up. Existing research supports the applicability of Social Cognitive Theory in this context. For example, Al-Noumani found that when patients' personal beliefs conflict with physicians' advice,⁶⁷ they are indeed more prone to cognitive biases, exaggerate perceived risks, and thereby reduce compliance with medical recommendations. These findings further validate the theoretical framework of this study and strengthen its argument. Therefore, failing to promptly identify and address patients' intolerance of uncertainty and the interpretive bias it triggers may further deteriorate the doctor-patient relationship, increase resistance to follow-up recommendations, and reduce treatment effectiveness. This is particularly crucial for healthcare providers, as they may overlook this important psychological dynamic in their practice.

Self-Compassion Can "Help" Patients to Some Extent

Within the framework of resource protection theory, self-compassion acts as a moderating variable that effectively alleviates the negative impact of IU. Specifically, self-compassion enhances patients' psychological resources, helping them better manage emotions and reduce the development of negative interpretation bias. Consequently, patients can maintain trust in medical guidance when facing uncertainty, thus avoiding the weakening of trust and the decline in treatment adherence to follow-up caused by cognitive bias. Research shows that high levels of self-compassion help reduce individuals' negative cognitive responses to stress, enhancing psychological resilience and adherence.^{72,73} However, for patients with low treatment adherence to follow-up, they may adopt alternative strategies to alleviate anxiety stemming from IU due to the necessity of resource protection. For example, when patients acquire alternative information via the Internet or social media that contradicts their physician's recommendations, this inconsistency may cause confusion or skepticism, further weakening their trust in healthcare professionals.⁷¹ Particularly when these alternative sources align more closely with patients' expectations or needs, they may be more inclined to trust this external information over the professional opinions of physicians. This is not merely a deviation in interpretation but

may lead patients to question medical authority, hindering their adherence to medical advice. Ultimately, the erosion of trust results in reduced treatment adherence to follow-up and impacts treatment efficacy. Therefore, improving patients' self-compassion level can effectively mitigate the negative impact of IU on interpretation bias and trust in physicians. Self-compassion helps patients better manage emotions and reduce negative interpretation bias when facing uncertainty, thus maintaining trust in medical personnel. This improvement in trust creates a more favorable follow-up environment, thereby enhancing treatment adherence to follow-up and ultimately promoting better long-term health outcomes.

Limitations and Future Study Directions

Several key limitations should be acknowledged in this study. The cross-sectional design precludes establishing a definitive causal relationship between IU and treatment adherence to follow-up, thereby limiting the understanding of their dynamic interaction. To address this, future longitudinal studies are recommended to validate these findings. Additionally, reliance on self-reported data may have introduced social desirability bias, particularly for variables like treatment adherence and self-compassion, as participants might report behaviors that align with socially expected norms. However, efforts were made to minimize this bias by ensuring the anonymity and confidentiality of responses, thus encouraging more honest and less socially influenced reporting. Despite these precautions, the possibility of social desirability bias remains a limitation that could affect the objectivity of the results. Thus, future research should incorporate more objective, experimental methods to enhance result accuracy.

While this study primarily explored the effects of IU, interpretation bias, and physician trust on treatment adherence to follow-up, other factors, such as personal characteristics and social support, likely also play a significant role. Further investigation into these variables is warranted to provide a more comprehensive understanding of their impact. Another limitation is the exclusive collection of negative interpretation scores, which may have led to data bias and limited the generalizability of the findings. However, considering the strong correlation between negative interpretations and adverse health behaviors, focusing on negative interpretations aligns with the research objectives. Despite these limitations, efforts were made to minimize bias through rigorous research design and analytical methods, ensuring the reliability of the findings. Although analysis of interpretations to explore their distinctive impact on treatment adherence to follow-up. This approach is well-supported by psychological theory and maximizes the study's effectiveness under the given constraints, providing clearer theoretical validation.

Although this study focused on IU, interpretation bias, and physician trust, the potential role of Langerian mindfulness in enhancing self-compassion and trust in medical professionals should be explored in future research. Langerian mindfulness, which emphasizes awareness of changing situations and flexibility in responses, may serve as an effective intervention to improve both self-compassion and patient trust.^{17,18} In clinical settings, healthcare providers could integrate Langerian mindfulness into their practice by encouraging patients to engage in mindfulness exercises that foster awareness of thoughts and flexibility in coping with uncertainty.^{17,18} Mindfulness-based interventions, such as guided meditation or reflective journaling, could help patients develop self-compassion and trust in their healthcare providers.^{74–77} Future studies could investigate the application of this mindfulness approach in clinical settings, contributing to enhanced treatment adherence and overall patient well-being.

In conclusion, these limitations do not significantly undermine the overall value of the study. The findings offer compelling evidence regarding the impact of IU on treatment adherence to follow-up and establish a solid foundation for future research.

Conclusion

The findings of this research reveal considerable variability in treatment adherence to follow-up among young and middle-aged patients newly diagnosed with pulmonary nodules, based on demographic factors such as gender, geographic location, and age. A significant association was found between patients' intolerance of uncertainty (IU) and their adherence to treatment, with self-compassion playing a mediating role in this relationship. Moreover, negative interpretation tendencies and trust in physicians were identified as sequential mediators linking patient IU to treatment adherence to follow-up. The analysis further indicated that self-compassion reduces the detrimental effects of IU on interpretation bias. In conclusion, the study sheds light on the underlying mechanisms by which IU impacts treatment adherence to follow-up. By examining the harmful influence of heightened IU on adherence from different angles—self-compassion, interpretation bias, and physician trust—this study provides valuable theoretical and practical insights. These insights are crucial for designing targeted interventions aimed at enhancing patient adherence and improving treatment outcomes.

To strengthen the validity and generalizability of the findings, future research should prioritize longitudinal studies to confirm the causal pathways identified in this study. These studies would provide more robust evidence on the long-term effects of IU, self-compassion, and trust on treatment adherence. Furthermore, the findings may have practical implications for both clinical practice and policy development. Clinicians could consider incorporating self-compassion-based interventions into treatment plans, especially for patients with high IU, to improve adherence to treatment. Policymakers should also recognize the influence of intolerance of uncertainty (IU) on patient adherence to treatment and follow-up care, as it can impact overall health outcomes. Understanding IU's role can inform the development of policies and resources that provide targeted support, particularly through Langerian mindfulness-based and self-compassion strategies. When combined with efforts to build trust in healthcare providers, these approaches could improve patient engagement and adherence to follow-up care. This study offers insights into how the negative effects of IU on treatment adherence can be mitigated.

Data Sharing Statement

The datasets generated and/or analyzed during this study are available from the corresponding author upon reasonable request.

Ethics Approval and Informed Consent

All participants and their legal guardians provided informed consent. The study was conducted in accordance with the ethical standards set forth by the WMA Declaration of Helsinki and received approval from the Ethics Committee of Henan Provincial People's Hospital under approval number 2022-93.

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Disclosure

The authors declare that there are no conflicts of interest.

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