

The Mediating Role of Cognitive Avoidance in the Relationship Between Intolerance of Uncertainty and Chronic Pain in Multiple Sclerosis Patients: A Structural Equation Modeling Approach

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ABSTRACT

Chronic pain is a prevalent and debilitating symptom in multiple sclerosis (MS). While psychological factors, such as intolerance of uncertainty (IU), are known contributors, the specific mechanisms underlying them are underexplored. This study aimed to investigate whether cognitive avoidance (CA) mediates the relationship between IU and chronic pain severity in this population. In this cross-sectional study, 339 patients with MS (151 men, 178 women) were recruited via convenience sampling from medical centers in Tehran, Iran. Participants completed the Intolerance of Uncertainty Scale (IUS), the Cognitive Avoidance Questionnaire (CAQ), and the Brief Pain Inventory-Short Form (BPI-SF). Data were analyzed using structural equation modeling (SEM). A partial mediation model demonstrated an excellent fit to the data (CFI = 0.99, RMSEA = 0.055, $\chi^2/df = 2.02$). The analysis revealed both a significant direct effect of IU on chronic pain and a significant indirect effect mediated by CA, which was confirmed via bootstrapping. The final model accounted for 13% of the variance in chronic pain. Our findings highlight the crucial role of cognitive-behavioral mechanisms in MS-related chronic pain. Individuals with higher IU tend to engage in cognitive avoidance, which exacerbates their pain, identifying CA as a key therapeutic target. Psychological interventions aimed at reducing avoidance and enhancing tolerance to uncertainty may therefore provide a promising approach to improving pain management and well-being in individuals with MS.

Keywords: Multiple Sclerosis, Cognitive Avoidance, Chronic Pain, Intolerance of Uncertainty.

1. Introduction

Multiple sclerosis (MS) is a chronic, immune-mediated, demyelinating disorder of the central nervous system characterized by inflammatory processes, neurodegeneration, and progressive disruption of neural transmission. The disease can affect motor, sensory, cognitive, autonomic, and emotional functioning, thereby imposing a multidimensional burden that extends substantially beyond neurological impairment. Symptoms may include fatigue, weakness, gait disturbances, visual problems, cognitive impairment, sexual dysfunction, sleep difficulties, mood disturbances, and pain, and their severity and configuration may vary considerably both between patients and across the course of illness within the same individual (Abou El-Maaty et al., 2024). Contemporary research has also emphasized the biological heterogeneity of MS, with combinations of inflammatory and protein biomarkers potentially contributing to diagnosis, prognosis, and variation in disease outcomes (Kodosaki et al., 2024). Although biomedical advances have improved diagnostic accuracy and disease-modifying treatment, the subjective burden of MS remains substantial because patients must continuously adjust to fluctuating symptoms, uncertain disease progression, and the possibility of future disability. Consequently, psychological processes affecting adaptation to uncertainty and symptom-related distress represent an increasingly important dimension of comprehensive MS care.

The unpredictable nature of MS is particularly relevant to psychological adjustment. Patients may experience periods of relative stability followed by unexpected relapses, new neurological symptoms, or gradual deterioration, often without being able to predict precisely when these changes will occur or what their long-term consequences will be. Such uncertainty can undermine perceived control and self-efficacy and complicate the development of stable coping strategies. Studies of psychological adaptation in MS indicate that personal coping capacities and psychological skills are closely associated with adjustment, particularly during the early stages of progressive disease (Bogosian et al., 2022). Similarly, illness perceptions, fatigue, locus of control, self-efficacy, and coping strategies appear to form interconnected psychological systems through which patients interpret and respond to their condition (Akbari Esfahani et al., 2024). The consequences of maladaptive adjustment are clinically important because emotional difficulties can affect quality of life independently of

neurological disability. Individuals newly diagnosed with MS or clinically isolated syndrome may already experience meaningful impairment in quality of life, indicating that psychological burden emerges early and cannot be understood merely as a consequence of advanced physical disability (Alschuler et al., 2022).

Among the psychological constructs that may be especially relevant to living with an unpredictable neurological illness is intolerance of uncertainty (IU). IU refers to a dispositional tendency to perceive uncertain, ambiguous, or insufficiently predictable situations as threatening, unacceptable, or difficult to manage. Individuals with high IU are more likely to interpret incomplete information negatively, anticipate adverse future events, and experience cognitive and emotional distress when certainty cannot be achieved. IU has increasingly been conceptualized as a transdiagnostic vulnerability factor because it contributes to anxiety across different clinical conditions rather than being restricted to a single psychiatric disorder. Its relationship with anxiety sensitivity and broader emotional vulnerability indicates that intolerance of uncertain future outcomes can intensify threat appraisal, worry, and maladaptive responses to distress (Allan et al., 2023). Psychometric research has also supported the applicability of IU assessment in neurological populations, demonstrating that the construct can be meaningfully measured following acquired brain injury and remains associated with emotional and functional outcomes in individuals coping with neurological uncertainty (Kusec et al., 2024).

IU is particularly salient in MS because uncertainty is embedded in virtually every level of the disease experience. Patients may be uncertain about whether symptoms indicate relapse, whether treatment will remain effective, how quickly disability may progress, whether work and family roles can be maintained, and how future independence may be affected. Recent evidence directly indicates that greater intolerance of uncertainty among patients with MS is associated with greater symptom severity and poorer disease self-management (Taskin Yilmaz et al., 2025). This association suggests that IU is not simply an emotional reaction to disease but may influence how individuals interpret symptoms, make health-related decisions, and engage in behaviors necessary for disease management. High IU may also magnify anticipatory distress regarding recurrence or deterioration. For example, fear of relapse in MS has been associated with intolerance of uncertainty, emphasizing that patients who find uncertainty especially

difficult may remain psychologically preoccupied with the possibility of renewed disease activity even during periods of clinical stability (Akboğa et al., 2025). These patterns suggest that IU may serve as a higher-order cognitive vulnerability through which the inherent unpredictability of MS is transformed into sustained emotional and somatic distress.

The importance of IU becomes even more apparent when considered alongside anxiety and depression, which are common and clinically consequential in MS. Anxiety and depressive symptoms can arise from the direct and indirect effects of neurological disease, uncertainty regarding prognosis, losses in functioning, social restrictions, and concerns about future disability. These emotional symptoms may in turn reduce subjective well-being, interfere with treatment engagement, and worsen perceived quality of life (Hanna & Strober, 2020). More recent evidence suggests that depression, anxiety, and cognitive impairment are often interconnected in MS, with psychological and cognitive symptoms potentially sharing biological, behavioral, and disease-related mechanisms (Margoni et al., 2023). Depression and anxiety can therefore interact with cognitive appraisal processes, making ambiguous bodily sensations or changes in functioning appear more threatening and less controllable. The substantial impact of these emotional comorbidities has led to increasing recognition that effective MS management requires attention to the psychological processes that sustain distress rather than focusing exclusively on neurological disease activity (Jellinger, 2024).

Chronic pain represents another major source of burden in MS and provides an important context in which the psychological consequences of uncertainty may become clinically visible. Pain in MS is heterogeneous and may include central neuropathic pain, painful tonic spasms, musculoskeletal pain arising from altered mobility or posture, headache, and other persistent pain syndromes. Its mechanisms can involve central nervous system lesions, altered nociceptive processing, secondary musculoskeletal strain, and psychological amplification of pain-related threat (Racke et al., 2022). More broadly, chronic pain is increasingly understood as a multidimensional experience shaped by interactions among biological, psychological, and social factors rather than as a direct reflection of tissue damage or neurological pathology alone (Cohen et al., 2021). Risk factors and comorbid psychological states, including anxiety, depression, maladaptive beliefs, sleep disturbance, and behavioral avoidance, may influence both

pain intensity and the extent to which pain interferes with daily life (Hebert et al., 2024). Consequently, examining pain in MS requires consideration not only of neurological injury but also of how patients cognitively and behaviorally respond to pain and its uncertainty.

The emotional consequences of pain in MS appear particularly substantial when pain becomes persistent. Patients experiencing chronic pain may report greater psychological distress, reduced functioning, and an increased emotional burden, with different pain diagnoses potentially associated with distinct psychological characteristics (Rivel et al., 2024). Pain also has important consequences for broader quality of life, and evidence among individuals with MS indicates that pain experiences coexist with personal, psychosocial, and even existential factors that influence adaptation to illness (Sparaco et al., 2022). Across chronic pain populations more generally, pain-related disability is determined not only by pain intensity but also by psychosocial characteristics, supporting the view that cognition and emotion contribute meaningfully to functional outcomes (Landmark et al., 2024). These findings are particularly relevant to MS because chronic pain occurs within a disease already characterized by uncertainty, fluctuating symptoms, and concerns about neurological decline, creating a context in which threat-oriented cognitive processes may become self-reinforcing.

One theoretical framework that may help explain these relationships is the fear-avoidance perspective on chronic pain. According to fear-avoidance models, pain is more likely to become disabling when bodily sensations are interpreted as threatening and generate fear, hypervigilance, catastrophic expectations, and avoidance. Although avoidance may initially reduce exposure to feared experiences, repeated avoidance restricts activity, reinforces beliefs about danger, and prevents corrective learning, thereby maintaining disability and distress. Contemporary work on chronic musculoskeletal pain emphasizes that fear and avoidance should be understood as dynamic behavioral processes that can substantially affect recovery and rehabilitation (Alaiti et al., 2025). Within this perspective, intolerance of uncertainty may intensify pain-related threat because individuals who cannot comfortably tolerate ambiguous sensations or uncertain consequences are more likely to interpret pain as a signal of potential deterioration. In MS, where a new sensation may plausibly be interpreted as evidence of relapse or disease progression, the relationship between IU and avoidance may be especially powerful.

Pain-related distress is also influenced by broader forms of psychological intolerance. Pain catastrophizing and distress intolerance, for example, have been associated with heightened pain and emotional reactivity, indicating that difficulty tolerating aversive internal experiences may amplify responses to painful stimulation (McHugh et al., 2020). Such findings support the possibility that IU contributes to pain not solely through explicit fear of disease progression but also by increasing sensitivity to ambiguity and reducing the capacity to remain engaged with distressing sensations, thoughts, and emotions. Individuals who perceive uncertainty as intolerable may attempt to control or escape internal experiences rather than processing them adaptively. This tendency becomes especially consequential when the source of uncertainty cannot be eliminated, as is often the case in MS. Repeated efforts to suppress distress or obtain complete certainty may therefore paradoxically sustain attentional focus on threat and increase perceived pain.

A central process through which this effect may occur is cognitive avoidance. Cognitive avoidance encompasses mental strategies used to reduce contact with unwanted thoughts, images, memories, emotions, or anticipated threats. These strategies may include thought suppression, distraction, substitution of distressing thoughts with less threatening material, suppression of emotionally evocative imagery, and avoidance of situations or information that might activate unpleasant cognitions. Although such strategies can provide short-term relief, their repeated use may prevent emotional processing and reinforce the belief that distressing thoughts or uncertainty are dangerous and unmanageable. Research on responses to intrusive autobiographical memories demonstrates that cognitive avoidance and brooding can become intertwined with depression and maladaptive appraisal processes (Mihailova & Jobson, 2020). Accordingly, cognitive avoidance is not merely the absence of engagement; it represents an active regulatory strategy that may maintain distress by preventing individuals from learning that difficult internal experiences can be tolerated without catastrophic consequences.

The relationship between IU and cognitive avoidance is consistent with contemporary cognitive models of anxiety and worry. Individuals high in IU are more likely to interpret uncertain problems negatively, doubt their problem-solving capacity, and anticipate unsuccessful outcomes. A negative problem orientation can therefore combine with pessimistic expectations to increase depressive and maladaptive cognitive responses (Chang, 2024). Evidence comparing

major models of worry further indicates that intolerance of uncertainty, negative problem orientation, and contrast-avoidance processes each contribute to the persistence of anxiety-related cognition (Llera & Newman, 2023). From this perspective, cognitive avoidance can function as an attempt to manage the aversive emotional consequences generated by uncertainty. Instead of confronting an uncertain situation or tolerating distressing thoughts, an individual may suppress them, distract attention, or engage in repetitive worry that creates an illusion of cognitive preparation while preventing fuller emotional processing.

Avoidance processes have also been demonstrated in populations coping with severe chronic medical illness. Among patients with advanced cancer, intolerance of uncertainty and experiential avoidance have been shown to interact in explaining emotional distress, illustrating how an inability to tolerate uncertain outcomes may translate into maladaptive attempts to avoid difficult internal experiences (Panjwani et al., 2024). Although cancer and MS differ substantially in pathophysiology and prognosis, both conditions confront individuals with uncertainty regarding symptoms, treatment response, future health, and functional capacity. The relevance of avoidance-based processes across chronic illnesses therefore supports examination of cognitive avoidance as a mechanism through which IU may contribute to distress in MS. Moreover, resilience research in chronic pain increasingly emphasizes that adaptation depends not simply on stable personal traits but on flexible cognitive, behavioral, interpersonal, and contextual resources that influence responses to ongoing adversity (Sturgeon et al., 2024). Cognitive avoidance may undermine such resilience by narrowing coping options and encouraging disengagement from distressing experiences rather than flexible adaptation.

In MS specifically, maladaptive cognitive processing may have particularly broad consequences because the disease can also involve impairments in executive and social-cognitive functioning. Evidence indicates that disruptions in executive functioning may contribute to difficulties in social cognition among individuals with MS (Pennington et al., 2024). Such impairments may reduce the efficiency with which patients regulate attention, reconsider threatening interpretations, or shift away from rigid avoidance strategies. At the same time, successful self-care in MS requires patients to interpret symptoms, adhere to treatment, engage in health-promoting behaviors, and maintain adaptive responses to changing physical conditions. Research on determinants of self-care behavior

has highlighted the multidimensional nature of these behaviors and the importance of psychological and contextual factors in their maintenance (Pourhaji et al., 2024). Thus, greater IU coupled with cognitive avoidance may interfere not only with emotional adaptation but also with effective symptom monitoring and self-management.

The possible relationship between cognitive avoidance and chronic pain is also supported by evidence concerning psychological interventions in MS. Mindfulness-based approaches, which encourage nonjudgmental awareness and reduced avoidance of internal experiences, have shown potential benefits for sleep-related difficulties among people with MS (Guarnaccia et al., 2023). Although such findings do not directly establish a causal effect on pain, they demonstrate that modifying one's relationship with distressing internal states may improve clinically relevant outcomes. Other nonpharmacological interventions, such as transcranial direct current stimulation, have been examined for physical outcomes including balance and gait, underscoring the diversity of approaches currently used to address functional limitations in MS (Nombela-Cabrera et al., 2023). However, physical interventions alone may not fully address the cognitive-emotional mechanisms that contribute to symptom amplification and disability. Greater understanding of these mechanisms could therefore complement neurological and rehabilitation strategies.

Taken together, existing evidence establishes separate links among MS-related uncertainty, emotional distress, chronic pain, and avoidance, but important gaps remain. IU has been related to symptom severity, disease self-management, fear of relapse, and other forms of psychological distress in MS (Akboğa et al., 2025; Taskin Yilmaz et al., 2025), while chronic pain research has repeatedly demonstrated that psychological characteristics influence pain intensity, emotional burden, and disability (Landmark et al., 2024; Rivel et al., 2024). Furthermore, theoretical and empirical research across anxiety, chronic pain, neurological disorders, and other chronic medical conditions supports the idea that avoidance processes may connect intolerance of uncertainty with adverse outcomes (Allan et al., 2023; Panjwani et al., 2024). Nevertheless, comparatively little research has directly examined whether cognitive avoidance represents a mediating psychological mechanism through which intolerance of uncertainty is associated with chronic pain among patients with MS. Clarifying this pathway is theoretically important because it can integrate cognitive models of uncertainty with fear-avoidance accounts of chronic pain, and clinically important

because cognitive avoidance may represent a more modifiable therapeutic target than the unavoidable objective uncertainty created by MS itself.

Therefore, the aim of the present study was to examine the mediating role of cognitive avoidance in the relationship between intolerance of uncertainty and chronic pain among patients with multiple sclerosis using a structural equation modeling approach.

2. Methods and Materials

2.1. Study Design and Participants

This study employed a cross-sectional, descriptive-correlational research design. The statistical population consisted of all patients with Multiple Sclerosis who visited the Kowsar Imaging Center and the Iran MS Society in Tehran during the previous year. The statistical sample consisted of 339 patients (151 men and 178 women) selected using a convenience sampling method. Participants reported the duration of their MS diagnosis across a range from less than 5 years to over 20 years. Following the rationale proposed by Kline (2015) for the use of structural equation modeling, a sample size of 339 was chosen to ensure a ratio of more than 20 participants for each of the 15 estimated parameters in the model.

2.2. Measures

Intolerance of Uncertainty Scale (IUS). The IUS is a 27-item self-report measure developed by Freeston et al. (1994) to assess individuals' tolerance for uncertain and ambiguous situations. The original scale uses a 5-point Likert scale (1 = Never to 5 = Always). In the Persian version utilized in this study, the response format was modified to an 11-point scale (0 = Never to 10 = Always) to enhance response precision. A Principal Component Analysis (PCA) on the current sample's data revealed a three-component factor structure: the stressful nature of ambiguous situations, a negative orientation toward unexpected events, and an ambiguous/uncertain future. The internal consistency coefficients (Cronbach's alpha) for these components in the present study were 0.92, 0.90, and 0.81, respectively.

Cognitive Avoidance Questionnaire (CAQ). The CAQ is a 25-item questionnaire designed by Sexton & Dugas (2004) to measure cognitive avoidance strategies. The original instrument employs a 5-point Likert scale (1 = Completely False to 5 = Completely True). Higher total scores indicate greater use of cognitive avoidance. The original study

reported high internal consistency ($\alpha = 0.95$) and good test-retest reliability ($r = 0.85$ over 6 weeks) (Sexton & Dugas, 2004). For the Persian version in this study, the response format was changed to an 11-point scale (0 = Completely False to 10 = Completely True). PCA results supported a two-component structure for the current sample: distraction and avoidance of threatening stimuli, and thought substitution and suppression. Both components demonstrated excellent internal consistency, with Cronbach's alpha coefficients of 0.94 and 0.92, respectively.

Brief Pain Inventory-Short Form (BPI-SF). The BPI-SF is a widely used 9-item inventory developed by Cleeland (1989) to assess the severity of chronic pain and its interference with daily functioning. Although initially designed for cancer patients, it is now broadly applied in chronic pain research. The inventory yields two primary scores: pain severity and pain interference. In the present

study, both the pain severity and pain interference dimensions showed good internal consistency, with Cronbach's alpha coefficients of 0.83 for each.

2.3. Data Analysis

Data were analyzed using structural equation modeling (SEM).

3. Findings and Results

Descriptive statistics for all measured variables are presented in Table 1. Prior to the main analysis, the assumptions for structural equation modeling were verified. Skewness and kurtosis values were within acceptable ranges for assuming univariate normality. Further diagnostics confirmed the normality of residuals, homoscedasticity, and the absence of multicollinearity.

Table 1

Descriptive Statistics for the Main Research Variables

	Mean	Standard Deviation	Skewness	Kurtosis
The stressful nature of ambiguous situations	45.71	19.21	0.06	-0.71
Negative orientation toward unexpected events	48.58	14.89	-0.24	-0.85
Ambiguous/uncertain future	33.24	10.53	-0.24	-0.4
Distraction and avoidance of threatening stimuli	82.88	26.22	-0.07	-0.46
Thought substitution and suppression	54.06	19.17	-0.15	-0.34
Pain severity	10.85	4.36	0.13	-0.54
Pain interference	7.05	3.5	0.31	-0.27

Table 2 displays the Pearson correlation matrix for the study variables. As hypothesized, the dimensions of Intolerance of Uncertainty demonstrated significant positive correlations with the facets of Cognitive Avoidance and Chronic Pain. Furthermore, Cognitive Avoidance was

positively and significantly correlated with both dimensions of Chronic Pain (pain severity and pain interference), supporting the prerequisite relationships for mediation analysis.

Table 2

Correlation Matrix of the Research Variables

	1	2	3	4	5	6	7
1. The stressful nature of ambiguous situations	1	0.69**	0.75**	0.44**	0.45**	0.23**	0.12*
2. Negative orientation toward unexpected events		1	0.74**	0.56**	0.39**	0.69**	0.69**
3. Ambiguous/uncertain future			1	0.45**	0.42**	0.18**	0.11*
4. Distraction and avoidance of threatening stimuli				1	0.79**	0.23**	0.23**
5. Thought substitution and suppression					1	0.23**	0.19**
6. Pain severity						1	0.45**
7. Pain interference							1

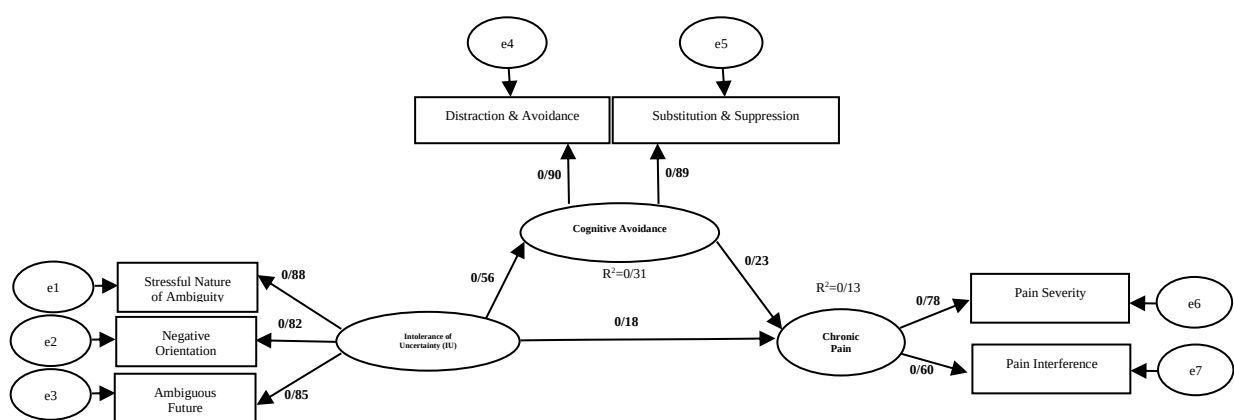
The hypothesized partial mediation model was tested using SEM to determine the mediating role of cognitive avoidance in the relationship between intolerance of uncertainty and chronic pain. The initial model demonstrated an excellent fit to the data, as indicated by multiple goodness-of-fit indices: $\chi^2(10) = 20.19$, $p < 0.05$; $\chi^2/df = 2.02$; CFI = 0.99; GFI = 0.98; AGFI = 0.95; RMSEA = 0.055, and PCLOSE = 0.36. Following the rationale that model fit can often be improved (Meyers et al., 2016), and based on a strong theoretical basis, a single post-hoc modification was made: a covariance path was added

between the error residuals of the 'distraction and avoidance' and 'negative orientation toward unexpected events' indicators.

The final model is depicted in Figure 1. All path coefficients in the model were statistically significant. The model successfully accounted for a significant portion of the variance in the endogenous variables. Specifically, intolerance of uncertainty explained 31% of the variance in cognitive avoidance ($R^2 = 0.31$), and together, intolerance of uncertainty and cognitive avoidance explained 13% of the variance in chronic pain ($R^2 = 0.13$).

Figure 1

The Hypothesized Partial Mediation Model in Patients with Multiple Sclerosis.



To test the significance of the mediating effect, a bootstrapping procedure with 5,000 resamples was employed. The results, shown in Table 3, revealed a significant indirect effect of intolerance of uncertainty on chronic pain through cognitive avoidance (Point Estimate =

0.29, 95% CI [0.008, 0.108]). As the 95% confidence interval does not contain zero, the mediating role of cognitive avoidance is confirmed as statistically significant. The model also supported a significant direct effect of intolerance of uncertainty on chronic pain.

Table 3

Bootstrap Results for the Indirect Path

Indirect Path	95% Confidence Interval		sig
	Lower Bound	Upper Bound	
The indirect effect of IU on Chronic Pain via Cognitive Avoidance	0.008	0.108	0.033

4. Discussion

The present study investigated the mediating role of cognitive avoidance in the relationship between intolerance of uncertainty and chronic pain among patients with multiple sclerosis (MS). The structural equation modeling results supported the proposed partial mediation model.

Specifically, intolerance of uncertainty was significantly and positively associated with cognitive avoidance, cognitive avoidance was significantly associated with chronic pain, and intolerance of uncertainty retained a significant direct association with chronic pain after cognitive avoidance was incorporated into the model. The bootstrapping analysis further confirmed that the indirect pathway from intolerance of uncertainty to chronic pain through cognitive avoidance

was statistically significant, demonstrating that cognitive avoidance partially explains how difficulty tolerating uncertainty may translate into a more severe experience of chronic pain. The model demonstrated excellent overall fit, with $\chi^2/df = 2.02$, CFI = 0.99, GFI = 0.98, AGFI = 0.95, and RMSEA = 0.055. Intolerance of uncertainty explained 31% of the variance in cognitive avoidance, while intolerance of uncertainty and cognitive avoidance together accounted for 13% of the variance in chronic pain. Thus, the findings indicate that intolerance of uncertainty has both a direct relationship with chronic pain and an indirect relationship operating through maladaptive cognitive avoidance processes.

The significant association between intolerance of uncertainty and chronic pain is theoretically and clinically meaningful in the context of MS. The course of MS is characterized by considerable unpredictability regarding relapse, symptom fluctuation, neurological deterioration, treatment response, and future functional independence. Individuals who have greater difficulty tolerating ambiguity may interpret these uncertainties as threatening and experience persistent anticipatory distress. The current finding is consistent with evidence showing that intolerance of uncertainty is an important psychological correlate of symptom burden and disease management in patients with MS. Taskin Yilmaz et al. found that intolerance of uncertainty was associated with symptom severity and disease self-management, suggesting that difficulty coping with unpredictable disease-related experiences may influence how patients perceive and respond to their symptoms (Taskin Yilmaz et al., 2025). Similarly, intolerance of uncertainty has been implicated in fear of MS relapse, particularly when patients interpret uncertain future disease activity as threatening and uncontrollable (Akboğa et al., 2025). These findings support the interpretation that intolerance of uncertainty may heighten vigilance toward bodily sensations and increase the likelihood that pain is evaluated as evidence of worsening illness or impending disability.

The direct relationship between intolerance of uncertainty and chronic pain can also be explained through broader models of anxiety and threat processing. Intolerance of uncertainty has been described as a transdiagnostic vulnerability that contributes to exaggerated threat appraisal, persistent worry, and difficulty disengaging from possible negative outcomes (Allan et al., 2023). In MS, bodily sensations are inherently difficult to interpret because they may represent transient discomfort, consequences of fatigue

or altered mobility, or potentially meaningful neurological changes. Patients characterized by high intolerance of uncertainty may therefore devote greater cognitive resources to monitoring these sensations, thereby increasing their salience and emotional significance. This interpretation is compatible with findings demonstrating that psychological risk factors and comorbid emotional problems contribute substantially to the burden and treatment complexity of chronic pain (Hebert et al., 2024). It is also consistent with research showing that anxiety and depression substantially affect well-being and quality of life in people with MS beyond the effects attributable to neurological disease itself (Hanna & Strober, 2020; Jellinger, 2024). Thus, the pain experienced by patients with high intolerance of uncertainty may reflect not simply greater nociceptive input, but a more threatening cognitive-emotional interpretation of painful and ambiguous bodily experiences.

The results also demonstrated that intolerance of uncertainty was significantly related to greater cognitive avoidance. This finding is consistent with cognitive models proposing that people who regard uncertainty as unacceptable are more likely to use mental strategies intended to reduce immediate contact with threatening thoughts and emotions. Cognitive avoidance may involve distraction, thought suppression, substitution of threatening cognitions, avoidance of distressing imagery, and efforts to prevent emotionally arousing thoughts from entering awareness. Although these strategies may temporarily decrease distress, they do not resolve the underlying source of uncertainty. Instead, they may reinforce the belief that uncertainty and distressing thoughts are intolerable. The present findings are compatible with evidence that intolerance of uncertainty contributes to maladaptive cognitive responses across anxiety-related conditions (Allan et al., 2023; Llera & Newman, 2023). Llera and Newman demonstrated that intolerance of uncertainty and negative problem orientation contribute meaningfully to anxiety-related processes, while avoidance of emotional contrasts may further maintain worry (Llera & Newman, 2023). In patients with MS, where uncertainty cannot be eliminated completely, habitual efforts to cognitively escape uncertain or threatening information may become especially persistent.

The relationship between intolerance of uncertainty and cognitive avoidance can also be interpreted in terms of negative problem orientation. Patients who perceive uncertain circumstances as dangerous and doubt their ability to manage future problems may progressively develop

pessimistic expectations and helplessness. Research indicates that negative problem orientation combined with pessimism can impose an additional burden on emotional functioning and contribute to depressive symptoms and maladaptive responses (Chang, 2024). In MS, patients may repeatedly encounter situations for which no immediate or definitive solution exists, including questions concerning future relapse, disease progression, treatment efficacy, employment, independence, and disability. Consequently, cognitively avoiding these possibilities can become an attractive short-term coping strategy. However, avoidance prevents realistic appraisal and emotional adaptation, potentially strengthening maladaptive beliefs about one's inability to cope. Findings regarding illness perception, self-efficacy, locus of control, fatigue, and coping among individuals with MS similarly indicate that cognitive interpretations of disease play an important role in psychological adjustment (Akbari Esfahani et al., 2024). The current results therefore extend this literature by demonstrating that intolerance of uncertainty may activate a specific maladaptive coping mechanism—cognitive avoidance.

An additional major finding was the significant positive relationship between cognitive avoidance and chronic pain. This association can be interpreted through contemporary fear-avoidance models of persistent pain. Within these models, attempts to avoid perceived threats may initially provide short-term relief but ultimately reinforce fear, hypervigilance, reduced engagement, and disability. Avoidance is therefore not merely a response to pain but can become a process through which the pain experience is maintained or amplified. Recent work on fear and avoidance in chronic pain emphasizes that avoidance behaviors can perpetuate pain-related disability by preventing corrective learning and maintaining beliefs that painful experiences are dangerous (Alaiti et al., 2025). Although cognitive avoidance differs from overt behavioral avoidance, a comparable process may occur internally. Patients who consistently suppress pain-related thoughts, distract themselves from threatening sensations, or avoid thinking about disease-related concerns may fail to process these experiences adaptively, thereby maintaining their emotional salience.

The association between cognitive avoidance and pain is also consistent with research examining distress intolerance and pain catastrophizing. Individuals who experience difficulty tolerating aversive internal states may react more strongly to pain and emotional stress, particularly when they

perceive painful experiences as uncontrollable or threatening (McHugh et al., 2020). Chronic pain itself is now recognized as a biopsychosocial phenomenon in which emotional, cognitive, behavioral, and interpersonal processes contribute to the persistence and functional impact of pain (Cohen et al., 2021). In the case of MS, neurological mechanisms unquestionably contribute to pain, including central neuropathic processes and musculoskeletal complications related to altered mobility (Racke et al., 2022). Nevertheless, the subjective severity and interference associated with pain are not determined exclusively by neurological damage. Psychosocial factors significantly contribute to pain-related disability in chronic pain populations (Landmark et al., 2024), and specific chronic pain diagnoses in MS have been associated with greater psychological and emotional burden (Rivel et al., 2024). The present findings therefore support an integrated interpretation in which cognitive avoidance acts alongside biological disease processes to shape the subjective experience of chronic pain.

The mediating effect of cognitive avoidance represents the most important contribution of the present study. The finding suggests that intolerance of uncertainty may increase chronic pain partly because patients respond to uncertainty with maladaptive cognitive efforts to suppress, avoid, or control distressing internal experiences. This pathway is consistent with findings from other chronic medical populations. Panjwani et al., for example, demonstrated meaningful relationships among intolerance of uncertainty, experiential avoidance, and emotional distress in individuals coping with advanced cancer (Panjwani et al., 2024). Although the medical characteristics of cancer and MS differ considerably, both conditions expose individuals to persistent uncertainties concerning symptoms, treatment outcomes, functional capacity, and future health. The present study extends this general mechanism to chronic pain in MS and suggests that avoidance may represent a psychological bridge between uncertainty-related vulnerability and somatic suffering.

Cognitive avoidance may maintain pain through several mutually reinforcing mechanisms. First, efforts to suppress threatening thoughts can paradoxically increase their accessibility, resulting in repeated monitoring for the very experiences the person wishes to avoid. Second, avoidance may reduce opportunities for emotional processing and habituation, preserving the perception that pain-related thoughts or sensations are dangerous. Third, avoidance can interfere with adaptive coping, problem solving, and

engagement in meaningful activity. Fourth, patients who repeatedly avoid disease-related cognitions may experience reduced perceived control, which can further increase anxiety and bodily vigilance. Research concerning cognitive avoidance and responses to intrusive memories similarly suggests that maladaptive appraisal and avoidance processes can contribute to persistent emotional disturbance (Mihailova & Jobson, 2020). These mechanisms are particularly plausible in MS because the illness itself cannot simply be avoided; consequently, unsuccessful efforts to cognitively escape disease-related uncertainty may intensify rather than resolve distress.

The observed mediation pathway is also compatible with the literature on adjustment and resilience in chronic illness and pain. Psychological adjustment to progressive MS is influenced by the availability of effective psychological skills and coping resources (Bogosian et al., 2022). Similarly, resilience in chronic pain is increasingly conceptualized as a dynamic process involving flexible emotional, behavioral, cognitive, and social adaptation rather than merely the presence of a stable personality trait (Sturgeon et al., 2024). Cognitive avoidance may represent the opposite of such flexibility because it narrows the range of responses available to individuals when they encounter difficult internal experiences. Rather than allowing patients to acknowledge uncertainty, reassess threats, and select adaptive actions, avoidance encourages disengagement from distressing cognitions. This may partly explain why intolerance of uncertainty indirectly contributes to pain. Patients who can tolerate uncertainty may remain more cognitively flexible and engage more effectively in disease management, whereas those who perceive uncertainty as intolerable may rely more heavily on avoidance and thereby experience greater psychological amplification of pain.

The present findings should also be considered in relation to the cognitive and functional difficulties associated with MS. Social-cognitive problems have been linked to executive dysfunction in MS, suggesting that some patients may experience difficulties in cognitive flexibility, inhibitory control, and effective management of complex social information (Pennington et al., 2024). Such difficulties could make disengagement from habitual avoidance strategies more challenging. At the same time, successful self-care in MS requires active symptom monitoring, treatment adherence, decision making, and adaptive responses to physical limitations. Psychological and contextual factors are therefore central to effective self-care behaviors (Pourhaji et al., 2024). If cognitive avoidance

reduces willingness to engage with threatening information concerning symptoms or disease management, it may contribute indirectly to poorer adaptation and heightened distress. This provides an additional explanation for why cognitive avoidance may be clinically meaningful beyond its immediate association with pain.

Nevertheless, the mediation was partial rather than complete, indicating that cognitive avoidance explains only one component of the association between intolerance of uncertainty and chronic pain. The direct pathway remained statistically significant, and the model explained 13% of the variance in chronic pain. This finding is theoretically reasonable because pain in MS arises from multiple interacting mechanisms. Biological factors such as demyelination, inflammatory activity, neurological lesions, and altered sensory processing remain important determinants of pain (Kodosaki et al., 2024; Racke et al., 2022). Emotional symptoms, fatigue, sleep disturbance, disability, coping, resilience, social resources, and illness perceptions may additionally influence pain outcomes. Studies have demonstrated substantial interactions among anxiety, depression, cognitive functioning, and disease-related outcomes in MS (Margoni et al., 2023), while quality of life may be compromised even relatively early in the disease course (Alschuler et al., 2022). Consequently, cognitive avoidance should not be considered the sole explanation for pain but rather one psychologically modifiable mechanism operating within a broader biopsychosocial system.

5. Conclusion

The findings have potentially important implications because psychological processes may offer intervention targets even when the objective uncertainty of MS cannot be eliminated. Interventions cannot guarantee freedom from relapse, eliminate all neurological pain, or provide complete certainty regarding future disease progression. However, they may modify how patients respond to uncertainty and distressing internal experiences. Mindfulness-based approaches may be especially relevant because they encourage observation and acceptance of thoughts and sensations rather than suppression or avoidance; mindfulness interventions have already demonstrated potential benefits for clinically relevant difficulties such as insomnia in people with MS (Guarnaccia et al., 2023). Similarly, approaches targeting psychological flexibility, cognitive reappraisal, tolerance of uncertainty, and adaptive

coping may interrupt the pathway through which uncertainty leads to avoidance and increased pain. This psychological perspective can complement physical and neurological interventions, including rehabilitation and other nonpharmacological approaches used to improve functioning among people with MS (Nombela-Cabrera et al., 2023). The current findings therefore support a multidisciplinary model of pain management in which psychological assessment and treatment are integrated with neurological and rehabilitative care.

Several limitations should be considered when interpreting the present findings. First, the cross-sectional descriptive-correlational design does not permit definitive causal or temporal conclusions. Although the proposed mediation model was theoretically grounded and demonstrated excellent statistical fit, it cannot establish that intolerance of uncertainty precedes cognitive avoidance or that cognitive avoidance subsequently increases chronic pain. Reverse or reciprocal relationships are also possible; persistent pain may increase uncertainty about disease progression and encourage greater cognitive avoidance over time. Second, participants were recruited through convenience sampling from the Kowsar Imaging Center and the Iran MS Society in Tehran, which may limit the generalizability of the findings to patients in other geographical areas, healthcare settings, cultural groups, or stages of MS. Third, the major study variables were measured through self-report instruments, making the findings potentially vulnerable to common-method variance, recall bias, and social desirability. Fourth, although the model identified statistically significant psychological pathways, it explained only a portion of the variance in chronic pain, indicating that additional biological, clinical, behavioral, and psychosocial factors were not incorporated into the model. Finally, the study did not separately evaluate possible differences according to sex, MS subtype, disease duration, disability severity, medication use, pain type, psychiatric symptoms, or other clinical characteristics that may modify the proposed relationships.

Future studies should employ longitudinal and prospective designs to establish the temporal ordering of intolerance of uncertainty, cognitive avoidance, and changes in chronic pain and to determine whether these relationships operate bidirectionally over the course of MS. Experimental and intervention studies would be particularly useful for determining whether reductions in intolerance of uncertainty or cognitive avoidance result in measurable improvements in pain severity or pain interference. Replication using

probability sampling, multicenter recruitment, and more geographically and culturally diverse samples would strengthen the external validity of the model. Future investigations should also examine additional mediators and moderators, including pain catastrophizing, psychological flexibility, experiential avoidance, emotion regulation, resilience, self-efficacy, illness perception, sleep disturbance, fatigue, anxiety, depression, and perceived social support. Multi-group structural models could determine whether the mediation pathway differs according to sex, MS subtype, disease duration, disability status, or specific forms of pain. Researchers may also combine self-report data with neurological indicators, clinician-rated disability measures, ecological momentary assessment, or objective behavioral measures to reduce common-method bias and provide a more comprehensive biopsychosocial explanation of pain in MS.

The findings suggest that psychological assessment should be incorporated more systematically into multidisciplinary pain management for patients with MS. Neurologists, psychologists, rehabilitation professionals, nurses, and pain specialists should consider screening patients with persistent pain for difficulty tolerating uncertainty and for avoidance-based cognitive coping patterns rather than assessing pain intensity alone. Psychological interventions may focus on helping patients identify thought suppression, excessive distraction, and other forms of cognitive avoidance; develop greater tolerance for ambiguous disease-related situations; differentiate realistic symptom monitoring from excessive threat vigilance; and increase flexible engagement with difficult thoughts, emotions, and bodily sensations. Cognitive-behavioral, acceptance-based, and mindfulness-oriented strategies may be adapted to the distinctive uncertainties associated with MS and integrated with medical and rehabilitative care. Psychoeducation should emphasize that uncertainty is an unavoidable element of a fluctuating neurological condition and that attempting to eliminate all uncertainty through avoidance may increase rather than decrease distress. Training healthcare professionals to recognize these cognitive-behavioral patterns may facilitate earlier referral for psychological intervention and contribute to more comprehensive management of chronic pain, emotional distress, self-management, and quality of life among individuals with MS.

Authors' Contributions

Authors equally contributed to this article.

Declaration

In order to correct and improve the academic writing of our paper, we have used the language model ChatGPT.

Transparency Statement

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Declaration of Interest

The authors report no conflict of interest.

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Ethics Considerations

The study protocol adhered to the principles outlined in the Helsinki Declaration, which provides guidelines for ethical research involving human participants.

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