

Understanding the sleep-pain relationship in patients with interstitial cystitis/bladder pain syndrome

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ABSTRACT

INTRODUCTION: Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic pelvic pain condition with critical symptoms of urinary urgency and frequency, persistent bladder-related pain, and reduced quality of life. Poor-quality sleep can lead to significant disturbances in daily life and increased pain in IC/BPS patients. Resilience, depressive symptoms, and pain catastrophizing have univariate associations with sleep and pain in IC/BPS, suggesting they may be mechanisms in this sleep and pain relationship.

METHODS: This online study recruited patients self-reporting a diagnosis of IC/BPS through support groups, social media posts (Facebook, Reddit, and Instagram), and urology clinic advertisements. Participants completed questionnaires on demographics, urologic symptoms, pain, pain catastrophizing, depressive symptoms, and resilience. Only those participants who met the RAND Interstitial Cystitis Epidemiology (RICE) criteria for IC/BPS diagnosis were included. A multiple mediation model was first examined, followed by a serial mediation model.

RESULTS: Seventy-four participants ($M_{\text{age}} = 47.0$, standard deviation [SD] 16.7, range 18–83 years) met inclusion criteria. A multiple mediation model showed greater sleep disturbance was associated with greater pain severity through depressive symptoms and pain catastrophizing, but not resilience ($b=0.79$, $\text{bootSE}=0.26$, bootCI [0.33, 1.35]). A serial mediation showed that the sleep-to-pain relationship had a significant indirect effect through pain catastrophizing and depressive symptoms ($b=0.78$, $\text{bootSE}=0.26$, bootCI [0.35, 1.32]).

CONCLUSIONS: Findings suggest depressive symptoms and pain catastrophizing may be important psychosocial mechanisms in the sleep-to-pain relationship. These results help guide future sleep and pain research in IC/BPS and aid in developing and refining treatments.

INTRODUCTION

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic pelvic pain condition marked by urinary urgency, urinary frequency, and persistent pain perceived to be related to the bladder, with no known etiology.^{1,2} Women with IC/BPS exhibit poor-quality sleep and shorter duration of sleep (≤ 6 hours).³ Compared with other chronic pain conditions (e.g., fibromyalgia), a cross-sectional study found that women with IC/BPS experience poorer sleep quality.⁴ Poor-quality or disturbed sleep can lead to significant disturbances in daily life, such as sleepiness, depression, reduced productivity, and poor quality of life.⁴ Research has demonstrated a bi-directional relationship between sleep and pain; however, the sleep-to-pain relationship is more established.⁵ In healthy patients, sleep loss increases pain sensitivity through lowered pain thresholds the following day.⁶ Further, sleep deprivation's effects accumulate and correlate with this lowered pain threshold.⁶

No comprehensive theoretical framework has described the complex sleep-pain relationship in chronic pain patients. The sleep-pain cycle comprises biological, psychological, and social variables that have unique and shared impacts on patient outcomes.⁵ A biopsychosocial disease model emphasizes the interconnection of biological, psychological, and social factors in understanding patient outcomes.⁷ The current study focused on the psychosocial aspect of this model to conceptualize how psychosocial variables (depressive symptoms, pain catastrophizing,

and resilience) may affect the sleep-pain relationship in patients with IC/BPS.

METHODS

Participants

Participants were included if they were at least 18 years old, reported a diagnosis of IC/BPS (and met RAND Interstitial Cystitis Epidemiology [RICE] Case Definition criteria), and could read and write in English. There were no exclusion criteria.

Procedure

After obtaining clearance from the Queen's University Research Ethics Board (#6037502), recruitment occurred from January to March 2023 through online media platforms (i.e., Facebook, Reddit, and Instagram) and advertisements in online support groups and urology clinics. Participants accessed the survey link or QR code via advertisements and submitted informed consent. The survey required 25–35 minutes and no incentives were offered.

Measures

DEMOGRAPHIC CHARACTERISTICS

Participants were asked to complete a self-report questionnaire identifying their age, gender, sex assigned at birth, and ethnicity. IC/BPS-specific demographic questions asked if the participant had received a previous IC/BPS diagnosis, the month and year the diagnosis was received, and if the participant was experiencing a symptom flare at the time of the survey response. Participants were also asked if they had ever been diagnosed with a sleep or mental health disorder and their current menstrual status.

IC/BPS CASE DIAGNOSIS

The RICE Case Definition Questionnaire is a reliable and validated measure to determine the validity of a participant's self-reported diagnosis of IC/BPS. This questionnaire has high sensitivity and yields few false negatives (IC/BPS cases are infrequently missed). This questionnaire classifies IC/BPS patients about pain and urgency criteria over five items.⁸ Participants included in the model had to meet the RICE criteria for diagnosis of IC/BPS by answering 'yes' to question 1 ('In the past six months, have you ever had a feeling of pain, pressure, or discomfort in your lower abdomen or pelvic area, that is, the part of your body that is above your legs and below your belly button?') AND answer, 'Pain, pressure, discomfort' to question 3 ('Would you say this

urge to urinate is mainly because of pain, pressure, or discomfort, or mainly because you are afraid you will not make it to the toilet in time to avoid wetting?') OR answer 10 to question 5 ('In the past three months [when you were having symptoms], how many times, on average, have you had to go to the bathroom to urinate during the day when you are awake?').

UROLOGIC SYMPTOMS

Symptom severity was assessed using the O'Leary-Sant Interstitial Cystitis Symptom Index (ICS_I) and Interstitial Cystitis Problem Index (ICPI), a reliable and validated measure for evaluating urinary and pain symptoms over the past month.⁹ The ICS_I measures the frequency of IC/BPS symptoms, while the ICPI assesses the magnitude of problems resulting from these symptoms. Both are four-item scales. Total scores, ranging from 0–20 and 0–16, respectively, are items summed with higher scores, indicating more severe symptoms and greater impact.

SLEEP QUALITY

The Pittsburgh Sleep Quality Index (PSQI), a reliable and validated 19-item self-report, was used to measure sleep quality and disturbances over the past month.¹⁰ The PSQI consists of seven component scores, measuring various aspects of sleep, such as latency, duration, disturbances, and daytime dysfunction. Total scores, ranging from 0–21, were obtained by summing scores, with higher scores indicating poorer sleep quality.

PAIN

The Short-Form McGill Pain Questionnaire (SF-MPQ), a reliable and validated self-report questionnaire, assessed sensory and affective pain dimensions and overall pain severity.¹¹ The questionnaire consists of 15 single-word descriptors, with 11 related to the sensory dimension of pain and four related to the affective dimension. Participants rate the applicability of each descriptor to their pain on a four-point scale. Total scores, obtained via summation, range from 0–45, with higher scores indicating greater pain.

DEPRESSIVE SYMPTOMS

The Patient Health Questionnaire-9 (PHQ-9), a reliable and validated nine-item self-report measure, assessed depressive symptoms.¹² Participants rated the frequency of experiencing nine main depressive symptoms based on the DSM-IV. Ratings ranged from 0 (not at all) to 3 (nearly every day). Total scores were obtained by summing the items from 0–27; higher scores indicated more frequent depressive symptoms.

PAIN CATASTROPHIZING

The Pain Catastrophizing Scale (PCS) is a reliable, validated 13-item questionnaire.¹³ Participants rated the frequency of experiencing specific feelings or thoughts during past painful experiences on a five-point scale. The PCS consists of three subscales (rumination, magnification, and helplessness) and a total score, all obtained by summing the items. Full scores range from 0–52, with higher scores indicate greater pain catastrophizing.

RESILIENCE

The Brief Resilience Scale (BRS) is a reliable and validated six-item self-report measure.¹⁴ Participants rated their agreement with statements on a scale of 1 (strongly disagree) to 5 (strongly agree). The scale included positively and negatively worded questions, with the negatively worded questions reverse-coded. Total scores were obtained by averaging all items; higher scores indicated greater resilience.

Data analysis

Survey data from the online Qualtrics software was imported into SPSS Statistics Version 27.^{15,16} Checks for irregularities, missing values, and outliers were conducted, with outliers identified using 3.5 standard deviations and visual inspection. Subscales, total scores, and demographic analyses were computed, and the ranges were examined for validity. Continuous variables were assessed for means, standard deviations, skewness, and kurtosis. Pearson correlations and reliability analyses were also conducted for the measures.

Model 4 of the PROCESS macro was used to examine whether sleep was associated with pain indirectly through depressive symptoms, pain catastrophizing, and resilience as parallel mediators.¹⁷ These relationships were modelled as sleep quality --> mediator --> pain severity. The independent variable was sleep quality, and the dependent variable was pain severity.

Model 6 of the PROCESS macro was used to examine a serial mediation model.¹⁷ Sleep quality was the independent variable, pain catastrophizing the first mediator, depressive symptoms the second mediator, and pain severity was the outcome variable. As such, this model went sleep quality --> pain catastrophizing --> depressive symptoms --> pain severity.

RESULTS

Participants

RICE Case Definition Questionnaire scores were computed to ensure participants met the IC/BPS diagnosis

criteria. Seven participants were excluded from the data set since they did not meet these criteria (N=74). In situations where participants completed some, but not all of the measures, their data were included in the analyses for the measures they had completed but excluded from analyses for those they did not complete.

Of the seventy-four participants (aged 18–83 years [mean 47.0, standard deviation (SD) 16.7]), most identified as female (n=69), four as male, and one as non-binary. Regarding sex assigned at birth (SAAB), 70 participants were born female, and four were born male. Most (87.8%) identified as European-Caucasian (n=65), eight with another ethnicity not listed, two as First Nations, Inuit, or Métis, one as Hispanic, one as Asian, and one preferred no answer.

In the SAAB as a female group, 43.5% (n=30) identified as premenopausal, 18.8% (n=13) to be perimenopausal/menopausal, and 37.7% (n=26) as postmenopausal. Additionally, 66.2% (n=49) of participants reported experiencing a symptom flare when they completed the study. Further, 73.0% (n=54) reported receiving treatment for their IC/BPS symptoms, whereas 18.9% (n=14) reported not receiving treatment. Lastly, most of the sample (n=34) reported having no mental health diagnoses or sleep disorder diagnoses (n=46), but a minority of the sample (n=13) reported having no comorbidities. Table 1 represents the sample's mental health diagnoses, sleep disorders, and comorbidities frequencies.

Descriptive statistics of all scales and subscales are presented in Table 2. Correlations between primary study variables were examined to identify significantly related variables (Table 3). There were no significant gender differences.

Multiple mediation model

A multiple mediation analysis using Model 4 of the PROCESS macro in SPSS was used to examine the indirect effect of depressive symptoms, pain catastrophizing, and resilience on the relationship between sleep quality and pain severity (Figure 1).¹⁷ There was a significant total effect ($b=1.35$, $SE=0.31$, $p<0.001$) and a significant overall indirect effect ($b=0.79$, boot standard error [SE]=0.26, boot confidence interval [CI] [0.33, 1.35]). The direct effect was not significant ($b=0.57$, $SE=0.33$, $p=0.0912$), indicating that sleep quality was not associated with pain severity when holding depressive symptoms, pain catastrophizing, and resilience constant.

Depressive symptoms had a significant indirect effect such that poorer sleep quality was associated with greater depressive symptoms ($b=1.09$, $SE=0.21$,

Table 1. Frequencies of mental health diagnoses, sleep disorder diagnoses, and comorbidities

	n	%
Mental health diagnoses		
None	34	45.9
Depression	27	36.5
Anxiety	27	36.5
Bipolar disorder	2	2.7
Post-traumatic stress disorder	16	21.6
Obsessive-compulsive disorder	5	6.8
Schizophrenia	0	0
Other	5	6.8
Sleep disorder diagnoses		
None	46	62.2
Insomnia	12	16.2
Sleep apnea	10	13.5
Restless leg syndrome	10	13.5
Other	6	8.1
Comorbidities		
None	13	17.6
Sjogren's	3	4.1
Lupus	0	0
Fibromyalgia	5	6.8
Neuropathies	7	9.5
Heart conditions (e.g., arrhythmia)	10	13.5
Endometriosis	17	23.0
Multiple chemical sensitivity	7	9.5
Other	44	59.5

Table 2. Descriptive statistics for all relevant scales and subscales

Scale	M	SD
ICSI	11.5	4.1
ICPI	10.5	3.8
PSQI	11.6	3.1
SF-MPQ	25.0	7.0
Sensory subscale	21.0	6.8
Affective subscale	8.0	2.4
Intensity subscale	10.0	5.6
PHQ-9	5.1	5.1
PCS	7.6	7.5
Rumination subscale	2.9	2.9
Magnification subscale	1.5	1.8
Helplessness subscale	3.2	3.5
BRS	3.1	0.9
MSPSS	4.9	1.3
Significant other subscale	5.4	1.7
Family subscale	4.7	1.6
Friends subscale	4.7	1.6

BRS: Brief Resilience Scale; ICSI: O'Leary-Sant Interstitial Cystitis Symptom Index; ICPI: Interstitial Cystitis Problem Index; M: mean; MSPSS: Multidimensional Scale of Perceived Social Support; PCS: Pain Catastrophizing Scale; PHQ-9: Patient Health Questionnaire-9; PSQI: Pittsburgh Sleep Quality Index; SD: standard deviation; SF-MPQ: Short-Form McGill Pain Questionnaire.

Serial mediation model

A serial mediation analysis using Model 6 of the PROCESS macro in SPSS was used to examine the indirect effect of sleep quality on pain through pain catastrophizing and depressive symptoms (Figure 2).¹⁷ There was a significant total effect ($b=1.35$, $SE=0.31$, $p<0.001$). The direct effect was not significant ($b=0.57$, $SE=0.33$, $p=0.0844$), such that sleep quality was not associated with pain when holding pain catastrophizing and depressive symptoms constant. There was a significant indirect effect ($b=0.78$, $bootSE=0.26$, $bootCI [0.35, 1.32]$), such that sleep quality was associated with pain severity through pain catastrophizing and depressive symptoms. Specifically, poor sleep quality was associated with greater pain catastrophizing ($b=1.28$, $SE=0.36$, $p<0.001$, $95\% CI [0.56, 2.00]$), greater pain catastrophizing was associated with greater depressive symptoms ($b=0.33$, $SE=0.06$, $p<0.001$, $95\% CI [0.22, 0.44]$), and greater depressive symptoms were associated

$p<0.001$, $95\% CI [0.68, 1.50]$), and greater depressive symptoms were associated with greater pain severity ($b=0.47$, $SE=0.20$, $p=0.0227$, $95\% CI [0.068, 0.87]$). Pain catastrophizing had a significant indirect effect such that poorer sleep quality was associated with greater pain catastrophizing ($b=1.28$, $SE=0.36$, $p<0.001$, $95\% CI [0.56, 2.00]$), and greater pain catastrophizing was associated with greater pain severity ($b=0.23$, $SE=0.12$, $p=0.0483$, $95\% CI [0.0018, 0.46]$). Lastly, the indirect effect of resilience was not significant. Poorer sleep quality was not associated with lower resilience ($b=-0.06$, $SE=0.03$, $p=0.068$, $95\% CI [-0.12, 0.004]$), and resilience was not associated with pain severity ($b=0.46$, $SE=1.24$, $p=0.712$, $95\% CI [-2.02, 2.94]$).

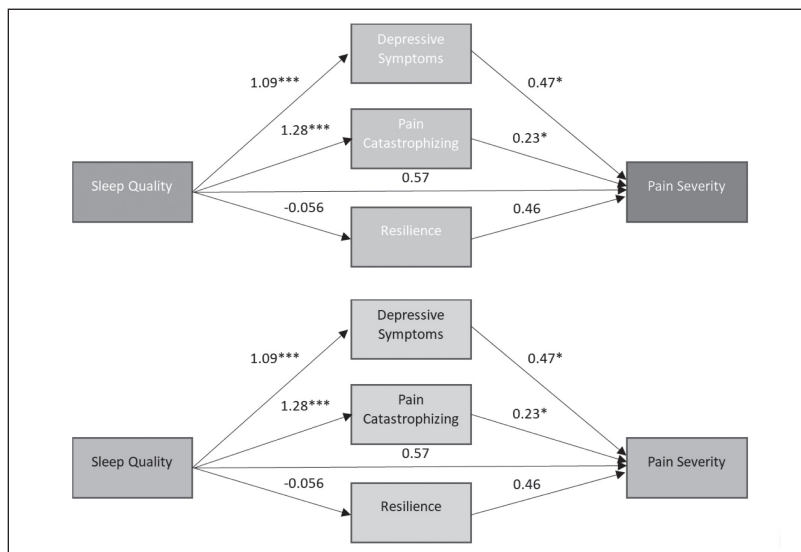


Figure 1. Depressive symptoms, pain catastrophizing, and resilience indirectly affect the sleep-to-pain relationship. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, $N = 74$, and all coefficients are unstandardized.

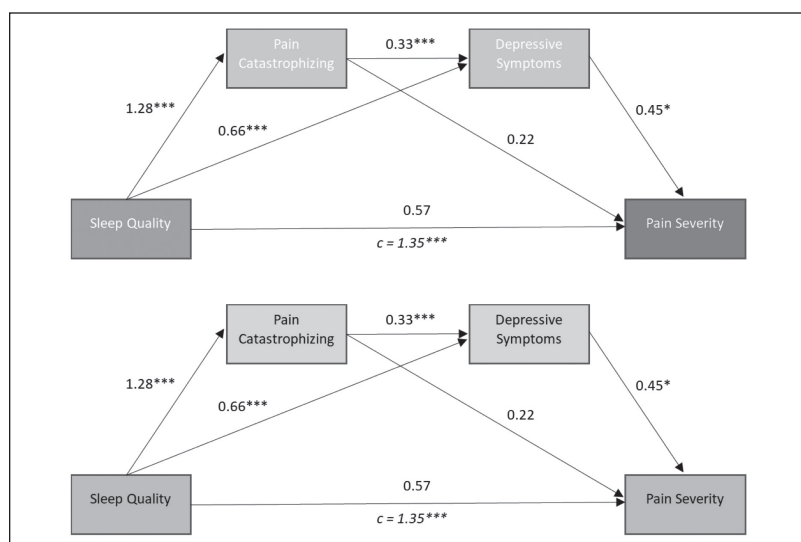


Figure 2. The serial mediation model shows that sleep quality affects pain severity through pain catastrophizing and depressive symptoms indirectly. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, and $N = 74$.

with greater pain severity ($b = 0.45$, $SE = 0.19$, $p = 0.0229$, 95% CI [0.064, 0.84]).

DISCUSSION

Depressive symptoms, pain catastrophizing, and resilience have been associated with sleep and pain, separately, in patients with IC/BPS. IC/BPS patients also report more depressive symptoms, sleep dysfunction, and decreased quality of life, with depression and pain catastrophizing being strongly linked to general pain and IC/BPS-specific symptoms.¹⁸

Depressive symptoms had a consistent indirect effect on the sleep-to-pain relationship. This sample reported moderate depressive symptoms, with just under 50% scoring in the none to mild depressive symptom range. Other IC/BPS research has reported similar depression ranges, with some samples having a higher representation of severe depressive symptoms.^{10,19}

Depression is a common comorbid condition of chronic pain conditions and has been established as having a strong relationship with sleep quality.^{20,21} As expected, the sleep and depressive symptom scores were strongly and significantly correlated. Depressive symptoms were the primary indirect effect of this study, suggesting that people with poor sleep might be at a higher risk for depressive symptoms and, in turn, greater pain severity. Individuals not experiencing depressive symptoms may still benefit from the study's findings, as they should promote good sleep to proactively mitigate any potential depressive symptoms not to risk greater pain. This result emphasizes the need for depressive symptoms to be assessed for and addressed in IC/BPS care to mitigate pain outcomes.

Feelings of helplessness and rumination towards pain characterize pain catastrophizing.¹³ For those with IC/BPS, pain catastrophizing is linked to greater pain, decreased quality of life, and more urologic symptoms.^{18,22} Additionally, studies in other chronic pain populations have found pain catastrophizing to mediate the relationship between self-reported sleep quality and pain intensity.²³⁻²⁵ Pain catastrophizing had a significant indirect effect on the sleep-to-pain relationship. A study focused on veterans with chronic pain also found pain catastrophizing to have a significant indirect effect on the sleep-to-pain relationship.²⁵ This suggests that people with poor sleep are at higher risk of pain catastrophizing and, in turn, greater pain severity.

Resilience, defined as the successful adaptation to challenging life experiences, is a well-established factor predicting pain outcomes and is negatively associated with pain and disease activity.²⁶⁻³¹ Resilience is also positively correlated with pain tolerance and duration to the pain threshold.²⁸ Concerning sleep, greater resilience has been associated with superior sleep quality and reduced latency to sleep.^{32,33} Resilience did not have a significant indirect effect on the sleep-to-pain relationship. Resilience was significantly and negatively correlated with pain, such that individuals who are more resilient may experience less pain. Although resilience is associated with sleep, the research on resilience and pain outcomes is much greater, fostering a more confident association between resilience and pain.²⁷⁻³¹

Sleep may not be associated with pain severity through resilience because resilience may primarily impact other dimensions of pain. Pain interference refers to the level of interference caused by pain to an individual's engagement in physical, cognitive, emotional, and recreational activities, in addition to their sleep and overall enjoyment of life.³⁴ Thus, greater resilience might lessen pain interference but not affect pain severity. Since resilience refers to an individual's ability to adapt to challenging experiences, it may pertain to a more psychological, as opposed to physiological, component of pain. This study assessed pain severity, not interference, possibly influencing the findings. Additionally, resilience may function more as a moderator than a mediator in the sleep-to-pain relationship. Nonetheless, this result implies that resilience-boosting interventions might not be vital for managing pain outcomes in those with IC/BPS.

The results of the serial mediation model showed that sleep quality is associated with pain through pain catastrophizing and depressive symptoms. This result suggests that poor sleep is associated with greater pain due to its impact on cognitions and mood, highlighting the importance for clinicians to identify patients with poor sleep as being at higher risk for pain catastrophizing, depressive symptoms, and in turn, pain. Additionally, this suggests that if patients are presenting with higher levels of pain, exploring and addressing these factors would be important. Further, in this model, the direct sleep-to-pain relationship became insignificant when considering these variables, emphasizing their impact on the sleep-to-pain relationship. Finally, this result underscores the importance of the biopsychosocial model in understanding how various biological, psychological, and social factors influence the experience of IC/BPS patients.

The results of the present study suggest that both depressive symptoms and pain catastrophizing contribute to the experience of IC/BPS patients by consistently having an indirect effect on the sleep-to-pain relationship. Thus, poor sleep quality may lead to greater depressive symptoms and greater pain catastrophizing, and in return, greater depressive symptoms and greater pain catastrophizing may lead to greater pain severity. This result has important clinical implications, as it suggests that patients could mitigate depressive symptoms and pain catastrophizing to reduce pain severity by increasing sleep quality.

Limitations and future research

There were variables omitted (e.g., socioeconomic status, childhood trauma) that could affect the sleep-pain

Table 3. Correlation matrix for all main measures

Measure	1	2	3	4	5	6
SF-MPQ	1					
BRS	-0.26*	1				
PHQ-9	0.59**	-0.46**	1			
PCS	0.51**	-0.43**	0.64**	1		
MSPSS	-0.13	0.35**	-0.27*	-0.085	1	
PSQI	0.41**	-0.23*	0.46**	0.30**	-0.16	1

* $p < 0.05$ (2-tailed), ** $p < 0.01$ (2-tailed). BRS: Brief Resilience Scale; MSPSS: Multidimensional Scale of Perceived Social Support; PCS: Pain Catastrophizing Scale; PHQ-9: Patient Health Questionnaire-9; PSQI: Pittsburgh Sleep Quality Index; SF-MPQ: Short-Form McGill Pain Questionnaire.

dynamic in IC/BPS, introducing potential confounders and limiting the depth of conclusions. Further, the study lacks information on patients' self-reported pain management strategies (i.e., use of narcotics, neuropathic pain agents, etc.), limiting the results by not accounting for non-compliance, narcotic abuse, uncontrolled pain thresholds, and existing pain flares, potentially impacting the severity of pain experiences.

Next, the use of sleep aids was not addressed among participants, limiting insights into how patients' utilization of sleep aids may have influenced reported sleep quality. Also, generalizability is constrained, as only English-speaking individuals were recruited. Further, the sample consists mainly of Western, educated, industrialized, rich, and democratic (WEIRD) participants. Additionally, the online self-reporting method might lead to misdiagnosis, although diagnoses were checked against the RICE Case Definition Questionnaire to combat such concerns.

Finally, the study's cross-sectional nature prevents drawing causal conclusions. A longitudinal approach is needed for causal insights into the sleep-pain relationship. Future research should explore this relationship's changes over time for improved patient care and differences in the relationship during flares vs. non-flare.

CONCLUSIONS

The current study contributes to understanding the dynamic sleep and pain relationship in patients with IC/BPS by showing how variables of depressive symptoms, pain catastrophizing, and resilience affect this relationship. The indirect effects of depressive symptoms and pain catastrophizing are particularly important: improving sleep quality could help in reducing depressive symptoms and pain catastrophizing and, in turn, reduce pain severity in this patient group.

COMPETING INTERESTS: Dr. Nickel has been an advisor/consultant for Immunotek, MicroGenDx, OM Pharma, Redleaf Medical, Valenca Int, and Zambon SpA; and has been involved in a European RCT study and a Canadian real-world study associated with Immunotek, and a study with MicroGenDx. Dr. Moldwin has been a PI and consultant for AbbVie and Ironwood Pharmaceuticals; and a consultant for Tringone Pharmaceuticals. Dr. Doiron has received research grants from Immunotek and Red Leaf Medical, both focused on UTI in women. The remaining authors do not report any competing personal or financial interests related to this work.

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