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## Psychosocial co-morbidities in Interstitial Cystitis/Bladder Pain syndrome (IC/BPS): A systematic review

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### Abstract

**Aims**—Psychosocial factors amplify symptoms of Interstitial Cystitis (IC/BPS). While psychosocial self-management is efficacious in other pain conditions, its impact on an IC/BPS population has rarely been studied. The objective of this review is to learn the prevalence and impact of psychosocial factors on IC/BPS, assess baseline psychosocial characteristics, and offer recommendations for assessment and treatment.

**Method**—Following PRISMA guidelines, primary information sources were PubMed including MEDLINE, Embase, CINAHL, and GoogleScholar. Inclusion criteria included: (i) a clearly defined cohort with IC/BPS or with Chronic Pelvic Pain Syndrome provided the IC/BPS cohort was delineated with quantitative results from the main cohort; (ii) all genders and regions; (iii) studies written in English from 1995 to April 14, 2017; (iv) quantitative report of psychosocial factors as outcome measures or at minimum as baseline characteristics.

**Results**—Thirty-four of an initial 642 articles were reviewed. Quantitative analyses demonstrate the magnitude of psychosocial difficulties in IC/BPS, which are worse than average on all measures, and fall into areas of clinical concern for 7 out of 10 measures. Meta-analyses shows mean Mental Component Score of the Short-Form 12 Health Survey (MCS) of 40.80 (SD 6.25,  $N = 2912$ ), where  $<36$  is consistent with severe psychological impairment. Averaged across studies,

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the population scored in the range seen in clinical depression (CES-D 19.89, SD 13.12,  $N=564$ ) and generalized anxiety disorder (HADS-A 8.15, SD 4.85,  $N=465$ ).

**Conclusion**—The psychological impact of IC/BPS is pervasive and severe. Existing evidence of treatment is lacking and suggests self-management intervention may be helpful.

### Keywords

anxiety; Bladder Pain Syndrome; depression; IC/BPS; Interstitial Cystitis; psychosocial; systematic review; trauma

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## 1 INTRODUCTION

Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS) is a debilitating, incurable, and costly pain condition affecting approximately 3-8 million individuals in the United States.<sup>1</sup> The economic burden of the condition is substantial, costing the healthcare system upwards of \$750 million a year.<sup>2</sup> Pain is the hallmark symptom of IC/BPS—which occurs in the region of the pelvis, urogenital floor, or external genitalia. In addition, most patients experience urgency, pressure/discomfort, and/or urinary frequency.<sup>3</sup> There is a limited understanding of IC/BPS pathophysiology and most treatments target symptom control. Biomedically based treatments currently lack effectiveness.<sup>4</sup> Between 1992 and 2001 the rates of physician office visits for IC/BPS tripled and outpatient hospital visits doubled.<sup>2</sup>

Evidence suggests psychosocial factors, such as comorbid anxiety, depression, quality of life, and trauma-related symptoms accompany and intensify the illness.<sup>5,6</sup>

Unaddressed psychosocial elements of chronic pain can shape patient perceptions and behavior, often leading to increased chronicity of symptoms and are associated with poorer functioning, adjustment, prognosis, and response to treatment.<sup>6-10</sup> These findings suggest not only a strong association, but also that psychosocial symptoms and bladder-specific symptoms reinforce one another.

Although there is a recognized need for psychosocial intervention as a first-line treatment for IC/BPS per national guidelines,<sup>4</sup> these interventions are difficult to implement in actual practice and as such they are underutilized. It is also unknown if the recommended therapies suggested in these guidelines sufficiently meet patient needs or whether patients with IC/BPS require a broader pain self-management approach as is used with other forms of chronic pain.<sup>11</sup> As there is paucity of randomized controlled trials evaluating how these interventions work and for whom, little is known about the impact of treating psychosocial factors on outcome.

While much is being learned about IC/BPS through Federally sponsored research (eg, Multidisciplinary Approach to the study of Pelvic Pain/MAPP<sup>12</sup>), including widespread psychosocial difficulties in IC/BPS,<sup>9</sup> there has yet to be a comprehensive review of the existing evidence examining psychosocial factors and IC/BPS. The objective of this review is to learn the prevalence and impact of psychosocial factors on IC/BPS, and assess baseline psychosocial characteristics. This is the first systematic review to our knowledge on the data available on the prevalence and impact of IC/BPS on psychosocial variables such as co-

morbid mental health conditions, psychological states, and quality of life. Having this information will help future researchers (i) capture relevant treatment outcomes; (ii) provide guidance on assessment domains; and (iii) increase knowledge to inform treatment approaches. This systematic review synthesizes the existing evidence of psychosocial factors associated with IC/BPS and, when possible, provides additional normative data as a tool for comparison. We then offer recommendations for assessment and treatment.

## 2 METHODS

### 2.1 Search strategy

We performed a systematic review of the literature in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Framework.<sup>13</sup> In consultation with a medical librarian, we established a review strategy to identify studies that differentiated cohorts with Interstitial Cystitis as either the primary study population or as a sub-cohort of analysis. The primary information sources were PubMed including MEDLINE, Embase, CINAHL, and Google Scholar.

Study inclusion criteria included: (i) a clearly defined cohort with Interstitial Cystitis or with Chronic Pelvic Pain Syndrome provided the Interstitial Cystitis cohort was delineated with quantitative results from the main cohort; (ii) all genders; (iii) studies written in English from 1995 to April 14, 2017; (iv) any study region; (v) quantitative report of psychosocial factors as outcome measures or at minimum as baseline characteristics. We focused on psychosocial attributes including trauma, anxiety, depression, panic traits, or quality of life measures. The use of validated instruments or self-report measures was not required but was noted when present in study results.

Search phrases were defined in MeSH and in Google Scholar and are shown below in Table 1.

Identified studies were screened for duplicates and subsequently underwent title and abstract review according to the criteria above. The resultant corpus of studies that fit our inclusion criteria were then reviewed in full-text. Data items were collected for each study: authorship, title, journal, year of publication, study design, study inclusion criteria, sample size, psychosocial measure(s) or prevalence, targeted outcome(s). One reviewer evaluated each study in detail. In the five cases where there was uncertainty regarding eligibility of the study for inclusion, additional reviewers (CW, WSR) were consulted.

### 2.2 Results synthesis

We evaluated eligible publications (total  $N = 34$ ) for both qualitative and quantitative data. The former incorporated a review of study design, methodology, and presence of an intervention designed to impact psychosocial measures or whether such measures were recorded as part of baseline characterization. Study limitations were also considered and recorded. Quantitative analyses included psychosocial measures and variances/standard deviations if reported.

For studies with quantified psychosocial measures ( $N = 17$ ), meta-analysis was performed with pooled statistics grouped by measure, for example, SF-36, and by targeted outcome, for example, trauma or abuse, if reported. We assumed equal population variances across studies given our inclusion criteria delineating the population with IC and therefore applied pooled variances with Bessel's correction to study results. We then compared pooled statistics against guidelines for clinical interpretation provided for each measure (see Table 3). Variables were calculated if more than one study used a given measure. Bias assessment was informed by the Cochrane Risk of Bias Tool though we note that the primarily observational nature of most research in this area coupled with relatively small sample sizes indicated common sources of bias and precluded rigorous application of this tool or others like Downs and Black.<sup>14</sup> These biases will be reviewed in aggregate (see section 3).

### 3 RESULTS

Using the inclusion criteria described above, the final number of reviewed articles was 34 out of 642 search results (see Figure 1). We have consolidated the details and primary findings of each study in Table 2. The review of psychosocial factors in IC/BPS is broken down into the following domains: depression, anxiety, stress/coping, trauma, quality of life, and demographic factors. We then detail findings of pooled statistics in available studies and place them in the context of population norms. Due to the limited evidence available on treatment studies, we do not qualitatively review them. Instead, we discuss the implications of their primary findings in our discussion.

#### 3.1 Depression

The impact of depression on IC/BPS was assessed in 16 of 34 studies. Study measures primarily involved self-reported symptoms of depression, with one study evaluating clinical diagnoses by chart review. Depression rates were elevated in all 16 studies, with prevalence rates ranging from 16 to 70%, fluctuating largely based on study type, sample size, and assessment method. Women with IC/BPS are between 2.4-6.6 times more likely to be diagnosed with depression than controls,<sup>15-17</sup> and four times more likely to use psychotropic medications. Depression is consistently associated with worsened symptom presentation, particularly in early stages of illness.<sup>16,17</sup> Patients who are depressed are less likely to work,<sup>6</sup> and are more likely to present with polysymptomatic complaints.<sup>9</sup> Helplessness, a symptom of depression, was associated with worsened mental functioning.<sup>18</sup> In a recent study, 23% of patients acknowledged experiencing suicidal ideation, which was associated with greater pain and worsened mental health functioning.<sup>19</sup>

#### 3.2 Anxiety and panic

Anxiety was assessed in 10 of 34 studies, with 8 assessing symptoms through self-report measures, 2 evaluating clinical diagnoses given during medical record review, and 1 structured and validated clinical interview assessing for the presence of an anxiety disorder. Prevalence rates of anxiety symptoms in IC/BPS ranged from 14 to 52%. Regarding diagnosed conditions, individuals are 4.37 times more likely to have a pre-existing anxiety disorder prior to developing IC/BPS<sup>20</sup> and are 2.4 times more likely to develop an anxiety disorder following IC/BPS diagnosis.<sup>16</sup> Similarly, in another study, panic disorder was

diagnosed in 26.9% of cases, indicating that women with IC/BPS are 4.1 times more likely than those with other urological disease to develop panic disorder in their lifetime— and to have first degree relatives that are twice as likely to have panic disorder.<sup>21</sup> Patients with anxiety also show increased urinary symptom severity and lower self-esteem.<sup>22</sup>

### 3.3 Stress and coping

Nine studies measured stress and coping by assessing catastrophic thought processes, <sup>18,19,23–26</sup> perceived stress,<sup>9,23,24</sup> and self-efficacy.<sup>27,28</sup> Catastrophizing, or an internal exaggeration of events, rumination, or sense of helplessness in response to pain, is consistently related to worsened outcomes in mental and physical functioning.<sup>18,19,25</sup> In addition, catastrophizing increases vulnerability to suicidal ideation.<sup>19</sup> Both genders show heightened generalized stress levels, often in spite of the severity of symptoms.<sup>23,26</sup> Those with greater self-efficacy experienced less pain and depression.<sup>28</sup>

### 3.4 Trauma sequelae

Six studies measured abuse prevalence via validated self-report,<sup>5,9,24,29</sup> non-validated questionnaires,<sup>30,31</sup> and clinical interview of trauma exposure.<sup>30</sup> One study measured dissociative tendencies.<sup>29</sup> Overall abuse prevalence rates range from 25 to 49%. Trauma and abuse prevalence rates range significantly by method of reporting and abuse type. For example, between 21 and 40% of patients endorsed exposure to traumatic events as a child on self-report questionnaires. When asked directly via clinical interview, this number increased significantly in one study,<sup>30</sup> while decreasing in another study when asked directly “were you abused as an adult/child,” without a definition of “abuse.”<sup>5</sup> Abuse in childhood and adulthood is more common in female patients.<sup>9</sup> The presence of sexual abuse has been associated with altered symptom presentation, where patients experiencing greater sensory pain,<sup>24,31</sup> less daytime frequency and nocturia, larger voided volumes,<sup>31</sup> and worsened sexual functioning<sup>31,32</sup>—although one study notes this relationship is at most very modest.<sup>24</sup>

### 3.5 Quality of life factors

Twenty-one studies included a measure of quality of life. This most often included a broad measure on different life areas, and in some cases more specific aspects of daily life including insomnia, social support, self-esteem, and sexual functioning. Overall physical and mental quality of life is significantly impacted across the population. Quality of life is often worsened with increased symptom severity and co-occurring psychological difficulties.<sup>6,23</sup> Self-esteem and social functioning are both significantly impacted by IC/BPS<sup>22</sup> when compared to controls. Impaired sexual functioning is a common occurrence in the population; however, there was evidence of hesitancy in reporting this to providers or on questionnaires.

### 3.6 Demographic factors

Age is a significant factor when considering the psychosocial impact of symptoms. Studies found that younger individuals have increased risk of developing psychological comorbidities and insomnia following IC/BPS diagnosis,<sup>16</sup> have significantly diminished quality of life,<sup>33</sup> and are at higher risk for depression in the earlier stages of illness.<sup>17</sup> This

was true of both genders. These individuals are also more likely to utilize healthcare services for depression and anxiety.<sup>16</sup> Gender was also shown to impact symptom presentation, although these results are mixed. Women are more likely to present with polysymptomatic complaints.<sup>9,23,34</sup> The examination of abuse prevalence has occurred predominately in females. In the most comprehensive psychological study to date, comparing gender, Naliboff et al<sup>9</sup> found that women are more likely to report early life and adult trauma exposure, greater helplessness, and poorer functionality than men—irrespective of symptom severity or age. Although there is less available information on men with IC/BPS, a large population-based study showed that younger men were at higher risk of developing depression following IC/BPS diagnosis.<sup>16</sup> Other studies showed no gender differences in mental health presentation.<sup>15</sup>

### 3.7 Quantitative analyses

Pooled population means and standard deviations for psychosocial variables are presented in Table 3, along with clinical cutoff and suggested interpretations for each measure. Results clearly demonstrate the magnitude of psychosocial difficulties in IC/BPS, which are worse than average on all measures, and fall into areas of clinical concern for 7 out of 10 measures when following guidelines for clinical interpretation (see Table 3). The population's baseline psychological functioning is considered "depressed" according to two commonly used measures to assess depression. For example, of 564 subjects provided with the Center for Epidemiological Studies of Depression, or CES-D,<sup>35</sup> the mean response was 19.89. The clinical "cutoff" for this measure indicating extremely likely depression is 16,<sup>35</sup> or 19 in chronic pain patients.<sup>36</sup> Patients are much more likely to have an anxiety disorder and have stress levels of clinical concern. Of 465 subjects administered the Hospital Anxiety and Depression Scale (HADS-A), the mean response was 8.15. On this measure, a score greater than "8" indicates a 78% likelihood of having Generalized Anxiety Disorder.<sup>37</sup> There is significant impairment in quality of life in both mental (MCS = 40.80 [6.25],  $N = 2912$ ) and physical (PCS = 42.37 [6.67],  $N = 2912$ ) functioning. For mental functioning, this is well below population averages, and approaching "severe psychological impairment."<sup>38,39</sup> Quality of life measures indicate that at baseline women are at significant risk of sexual dysfunction (FSFI = 16.37, SD 8.12,  $N = 926$ ). Although Catastrophizing scores were elevated compared to population norms, the average scores of the two scales did not fall in the range of clinical concern.

**3.7.1 Risk of bias in reporting and study limitations**—Evaluating the psychosocial aspects of IC/BPS remains a relatively new area of study. There are limitations to note about the current literature. The most common method of evaluation was via self-report measures. These assessments cannot make definitive psychological diagnoses and are generally used as screening tools. Assessments given also lacked in consistency, making a collective analysis of studies difficult. Some of these measures did not adequately capture the outcomes assessed. For example, two used the Medical Outcomes Survey<sup>39</sup> sexual functioning scale, which does not measure sexual pain—a common experience impacting sexual functioning in IC/BPS. Some assessments suffered from a low response rate, (eg, Female Sexual Functioning Index<sup>40</sup> in mailed questionnaires from studies), and used measures lacking in validity.<sup>30,41</sup> There are concerns of under-reporting with trauma, abuse, and sexual



dysfunction due to discomfort with disclosure.<sup>5,30</sup> Roughly half of the studies lacked control groups. Sample sizes of clinical cohort studies were low in many of the studies reported. Data collected were often in convenience samples, with primarily white women in tertiary care centers. Many assessments were observational at one time point. The majority of studies cited did not follow patients over time. Even the treatment studies listed had limited, short-term follow-up. The three RCTs reported were not adequately powered to reliably assess for treatment effects.

## 4 DISCUSSION

This study is the first to provide a comprehensive review of the existing evidence evaluating psychosocial factors in IC/BPS. We reviewed 34 studies to provide a synthesis of the literature and guidance for future studies.

The psychological and social impact of IC/BPS is pervasive. There is significantly increased likelihood of an anxiety or depressive disorder both preceding and following IC/BPS diagnosis. Symptoms of anxiety, depression, and generalized stress, and increased suicidal ideation are paramount. Individuals are more likely to engage in catastrophic thought processes, which globally worsens functioning. IC/BPS has a detrimental impact on quality of life, self-esteem, and social functioning. Pooled statistics indicate that at baseline, mean scores on measures of anxiety, depression, and stress fall in areas of clinical concern as defined by their clinical interpretation guidelines (see Table 3).

### 4.1 Implications for assessment

In future studies we strongly recommend using validated measures to reliably capture psychosocial symptoms and diagnoses. When possible, evaluating psychological disorders associated with IC/BPS is best accomplished through a validated clinical interview. This was performed in one of the studies reviewed,<sup>21</sup> and will help provide the most accurate and reliable assessment of conditions beyond screening measures. In Table 3, we provide an overview of assessments most commonly used for psychosocial variables in IC/BPS, with guidelines for clinical interpretation. It is our hope that this can serve as a guide to future researchers, while also providing benchmarks for clinicians and further study. Table 4 outlines recommendations for assessment of pain in urologic disease provided by Williams. In addition to pain symptoms and medical co-morbidity, a comprehensive assessment includes affective vulnerability, patient beliefs and attitudes, and a patient's environment/social relationships. Many of the recommended assessments in Table 4 were not available for meta-analysis (used in <2 studies reviewed) or had not been used. In the future we recommend expanding on current research by using this reference as a guideline to structure a comprehensive assessment in clinical studies of IC/BPS.

**4.1.1 Trauma exposure**—While a relationship between trauma exposure and IC/BPS has been established in studies to date, the nature and impact of the association has yet to be fully elucidated. Future studies are in need of comprehensively assessing trauma across the lifespan, and simultaneously assessing active symptoms of post-traumatic stress disorder (PTSD). Of the studies reviewed, no studies evaluated active symptoms of PTSD. Post-

traumatic stress is known to exacerbate and maintain pain symptoms, and untreated PTSD has the potential to significantly impact the treatment course.

In one study, 29 of 30 women with childhood sexual abuse did not report this to their doctor.<sup>5</sup> Abuse exposure should be routinely assessed in clinical settings. As this is a difficult topic to broach with patients, a more appropriate screening measure may be to evaluate symptoms associated with trauma exposure—as opposed to direct questioning. This is employed in primary care settings with measures such as the four-item Primary Care—PTSD Screen (PC-PTSD<sup>42</sup>) and may reduce discomfort with direct disclosure.

## 4.2 Treatment implications

The demographic findings detailed above suggest that the early stages of illness are a particularly vulnerable period. Early access to psychological intervention may interrupt the development of these conditions, which could have important implications for illness prognosis. Gender differences may also impact symptom presentation and treatment approach. A recent review examining Chronic Prostatitis/Chronic Pelvic Pain Syndrome (CP/CPPS) found elevated prevalence rates of depression and anxiety disorder, but not panic disorder among patients.<sup>43</sup> This suggests that treatment approaches may have different targets of intervention depending on gender— however, further studies are needed to clarify these differences.

From evidence provided in this review, it is clear that untreated psychosocial factors worsen symptom presentation and prognosis. Untreated psychosocial co-morbidities may significantly impact the treatment process as well. Depressed patients are known as less likely to follow treatment recommendations. Helplessness and Catastrophizing influence patient behavior, lack of agency, and over-reliance on providers. Patients who experience anxiety may avoid procedures. For a patient with a sexual abuse history and/or PTSD, routine exams, urologic diagnostic procedures, and/or manual physical therapy have the potential to be re-traumatizing.<sup>44</sup> Accompanying recommendations from the AUA regarding first-line interventions for IC/BPS, the most recent National Pain Strategy<sup>45</sup> highlights the importance of taking an integrated, multimodal approach to managing pain in order to address the biopsychosocial factors influencing pain. The inclusion of a mental health provider into a multimodal treatment plan for IC/BPS has the potential to improve symptoms, quality of life, and treatment adherence.

## 4.3 Findings of self-management interventions

Of the three investigations to date, there are initial indications that self-management strategies have the ability to significantly improve symptoms and wellbeing in IC/BPS. Each study utilized a different approach—guided imagery/self-hypnosis,<sup>27</sup> mindfulness,<sup>46</sup> and online health education.<sup>47</sup> Although these investigations were all pilot studies and had limited follow-up, the findings are promising. Those treated reported significant reductions in pain and urinary urgency,<sup>46,47</sup> had greater perceived control of symptoms,<sup>46</sup> and better healthcare outcomes than controls.<sup>47</sup> The impact of these interventions on psychological states and co-morbidity has yet to be assessed.



A large proportion of the studies in this review urge the integration of psychological assessment and management into care plans for IC/BPS. Psychosocial self-management interventions could benefit patients through bolstering self-efficacy and increasing social support—which are known to buffer the impact of symptoms,<sup>28,48</sup> by improving treatment adherence,<sup>33</sup> and by reducing the impact of psychological co-morbidities that intensify the illness. These interventions may also be preferable as patients are often not responsive to psychotropic medications.<sup>15</sup> As psychological distress occurs across patient phenotype,<sup>9,26</sup> and many patients with only moderate symptoms have significant psychological burden,<sup>9,49</sup> patients at all stages of the illness could benefit. A recent survey conducted in collaboration with the Interstitial Cystitis Association ( $N=1982$ <sup>50</sup>) revealed that there is significant interest in and perceived benefits of employing self-management strategies such as stress reduction, sleep hygiene, relaxation, and meditation as well as engaging in active coping strategies to alleviate symptoms. This is a new area of clinical investigation with significant potential which patients are open to. Future well-controlled studies with larger sample sizes, comprehensive assessment, and long-term follow up are indicated.

#### 4.4 Strengths and limitations of review

This study accumulates previous literature and presents the best available evidence for the associations between and impact of psychological co-morbidities and IC/BPS. A strength of the current study is its comprehensive and reproducible search strategy. A limitation of this review is our inability to perform a true meta-analysis due to the limited literature available. Future studies are needed with longer-term follow-up and larger sample sizes. In addition comprehensive psychosocial assessment, including an assessment of PTSD symptoms is recommended. We believe that continued self-management intervention research is necessary based on the preliminary information available. We suspect that given the emerging evidence of a patient phenotype, interventions will likely need to be tailored to patient presentation.

The study of IC/BPS has largely been limited to females. As research is leaning toward conceptualizing IC/BPS and CP/CPPS as a unified condition (“UCPPS”<sup>12</sup>), examining the literature in both conditions may provide more information regarding gender differences and treatment individualization.

## 5 CONCLUSION

The psychological impact of IC/BPS is pervasive and severe. Existing evidence of treatment is lacking and suggests self-management intervention may be helpful.

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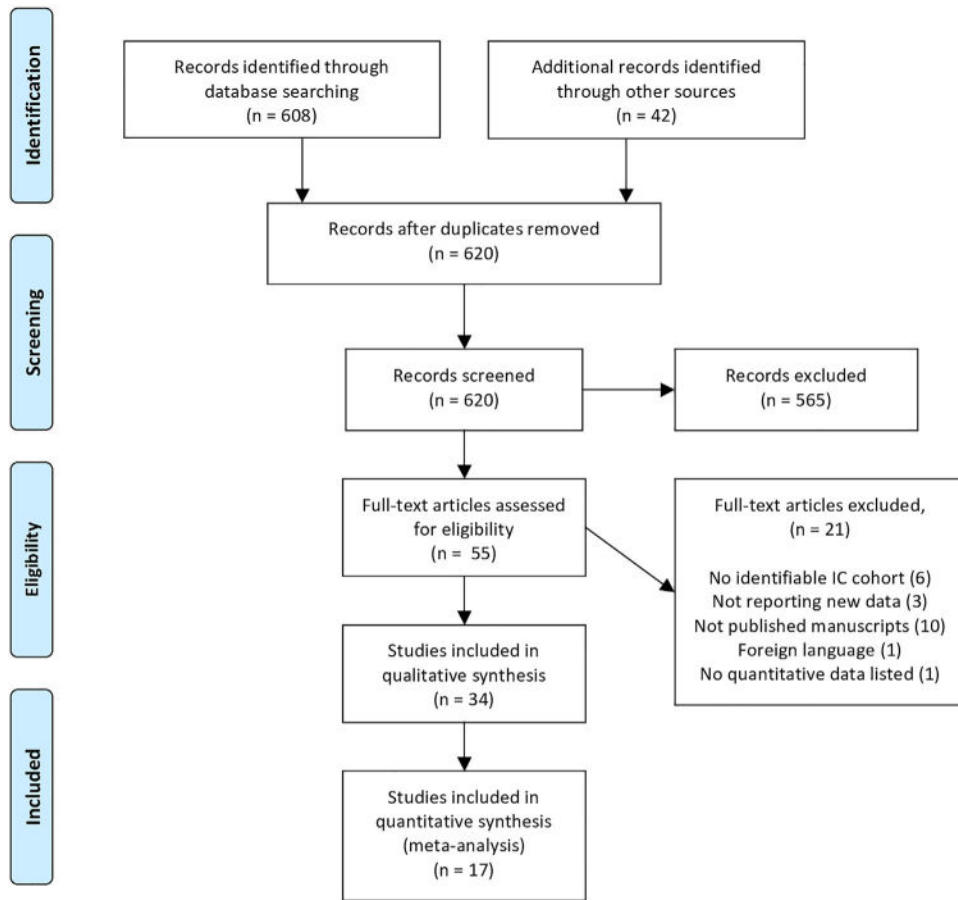
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**FIGURE 1.** Flow diagram per PRISMA (2009). Adapted from *PLoS Med.* 2009;6:e1000097



TABLE 1

## Search phrases by information source

Information source	Search phrase
PubMed, MEDLINE, Embase, CINAHL	("Cystitis, Interstitial" OR interstitial cystitis OR bladder pain syndrome OR mapp network OR chronic prostatitis with chronic pelvic pain syndrome OR chronic pelvic pain syndrome) AND ("Anxiety" OR anxiety OR "Depression" OR "Depressive Disorder" OR depression OR "Sleep Initiation and Maintenance Disorders" OR insomnia OR "Quality of Life" OR "Stress Disorders, Post-Traumatic" OR quality of life OR post-traumatic stress disorders OR "Health Promotion" OR "Psychology" OR psychosocial OR health promotion OR psychology) AND (Clinical Trial OR Comparative Study OR Evaluation Studies OR Meta-Analysis OR Observational Study OR systematic). NOT (drugs OR medications OR prescriptions OR pharmaceuticals)
Google scholar (title search only)	Search #1: Interstitial cystitis depression OR anxiety OR trauma OR abuse OR "post traumatic stress disorder"
	Search #2: bladder pain syndrome OR depression OR anxiety OR trauma OR "post traumatic stress disorder"

TABLE 2

Summary of reviewed studies (N = 34)

Author	Sample N	Female	Male	Race	Study type	Intervention	Relevant outcomes	Measure type	Primary findings
Carrico et al <sup>27</sup>	30 IC/BPS	100	0	100% w	RCT—Pilot	Guided imagery (N=15) vs resting (N=15)	Overall improvement (GRA), IC/BPS symptoms, self-efficacy (ICSES)	Validated self-report	45% of treatment group reported "moderate or marked improvement," significant reductions in pain and urgency
Chiu et al <sup>29</sup>	97 IC/BPS, 43 AC	100	0	NR	Observational cohort	N/A	Trauma prevalence (BBTS) * depression (BDI-II), anxiety (BAI), dissociation (TDS)	Validated self-report	IC/BPS group showed significantly higher rates of abuse, depression, and anxiety; relationships intensified by presence of childhood trauma by close others
Chuang et al <sup>16</sup>	185 IC/BPS, 370 HC	73	27	NR (Taiwanese sample)	Retrospective cohort	N/A	Depression, anxiety, insomnia	Chart review	Those younger are at higher risk for developing psychological comorbidities and healthseeking behavior for these comorbidities, males at higher risk, urging integrative care with psychologists early to interrupt this development
Chung et al <sup>20</sup>	396 IC/BPS, 1980 HC	100	0	NR (Taiwanese sample)	Retrospective cohort	N/A	Anxiety disorder diagnosis	Chart review	IC/BPS 4.37X more likely to have anxiety disorder, even after controlling for medical comorbidities
Clemens et al <sup>15</sup>	111 IC/BPS, 174 CP/ CPPS, 247 HC	39	61	83% W, 14% non-white	Case-control	N/A	Depression (PHQ-9), anxiety, mental health diagnosis	Validated self-report	Higher rates of psychological comorbidity in IC/BPS and CPPPS; no gender difference; Anxiety and Depression may be difficult to treat due to still having symptoms in spite of medications
El Khoudray et al <sup>48</sup>	41 IC/BPS	100	0	70.7% W, 29.3% non-white	Observational cohort	N/A	QOL (SF-36), IC/BPS symptoms	Validated self-report	Symptom severity associated with worsened pain, health, and mental health; being unmarried significantly related to symptom severity and worsened QOL; emphasizes role of social support
Fazio et al <sup>51</sup>	60 IC/BPS	94	6	94.1% W	Observational cohort	N/A	Personality assessment (MMPI-II)	Validated self-report	Authors believe 25% of sample may represent a somatization disorder; Note high overall distress and malaise that co-occurs with having this condition and need for psychological management as a part of care plan

Author	Sample N	Female	Male	Race	Study type	Intervention	Relevant outcomes	Measure type	Primary findings
Goldstein et al <sup>5</sup>	141 IC/BPS	100	0	NR	Observational cohort	N/A	Depression (BDI-II), abuse prevalence (DAQ)	Validated self-report	Significant associations between depression, abuse and IC/BPS. Significant decline in reported abuse when asked directly by male provider
Kanter et al <sup>16</sup>	20 IC/BPS	100	0	70% W, 10% Nat-Am, 5% Asian, 15% Other	RCT	MBSR (N=8) vs TAU (N=11)	Overall improvement, QOL (SF-12), IC/BPS symptoms, sexual functioning (FSFI)	Validated self-report	With MBSR, patients felt more empowered to control pain, improved self-efficacy, reductions in symptom reporting. No differences in QOL or sexual functioning between groups
Kim and Heitkemper <sup>52</sup>	130 IC/BPS, 168 HC	100	0	NR (Korean sample)	Observational cohort	N/A	QOL (HRQOL), depression (KGDS)	Validated self-report	IC/BPS symptoms associated with worsened physical interference, increased psychological distress, and lower QOL
Konkle et al <sup>49</sup>	3674 IC/BPS	100	0	74.7% W, 9.9% A-F-Am, 10.8% Hsp., 4.7% Other	Observational cohort	N/A	QOL (SF-36), prevalence of panic attacks	Validated & non-validated self-report	Community and clinical cohorts similar regarding symptom burden, community cohort significantly more distressed (although had less severe symptoms)—attributed to lack of treatment and not getting psychological or coping benefits to reduce the impact of symptoms
Lai et al <sup>23</sup>	233 IC/BPS, 191 CP/PPS (UCPPS)*	55	45	89% W, 11% non-white	Observational cohort	N/A	QOL (SF-12), anger (PROMIS), stress (PSS), coping (CSQ), depression/anxiety (HADS)	Validated self-report	Painful filling and urgency in females associated with increased depression, negative affect, worsened quality of life, and increased rates of overlapping conditions
Lee et al <sup>47</sup>	319 IC/BPS	86	14	NR (Taiwanese sample)	Observational cohort	N/A	QOL	Validated self-report — partial questions given	80% of sample reported sleep disturbance, 66% interference with work, 58% impacted sexual functioning
Lee et al <sup>47</sup>	65 IC/BPS	NR	NR	NR	RCT	Online health education (N=40) vs TAU (N=40)	QOL (SF-36)	Validated self-report	Health education showed significantly improved outcomes, QOL, alleviated symptoms at 8 weeks
Michael et al <sup>63</sup>	99 IC/BPS, 98925 HC	100	0	NR	Case-control	N/A	QOL (SF-36)	Validated self-report	In IC/BPS, QOL especially limited in psychosocial dimensions, such as vitality and mental health when compared to other health conditions
Naliboff et al <sup>9</sup>	233 IC/BPS, 191 CP/PPS(UCPPS),* 417 HC	55	45	89% W, 11% non-white	Case-control	N/A	QOL (SF-36), depression/anxiety (HADS), trauma prevalence (CTS), stress (PSS)	Validated self-report	Gender differences may impact assessment and treatment approach. Women show increased reports of overlapping symptoms, early life and adult trauma, and less

Author	Sample N	Female	Male	Race	Study type	Intervention	Relevant outcomes	Measure type	Primary findings
Nickel et al <sup>35,53</sup>	128 IC/BPS	91	9	NR	Retrospective analysis of RCT	PPS	QOL (SF-12), insomnia (MOS-Sleep/Partial), sexual functioning (MOS-SexFn)	Validated & non-validated self-report	control over pain and lower physical quality of life than men. Women with IC/BPS reported significantly greater childhood and adult trauma compared with controls. Differences in trauma and symptoms were not due to symptom severity or age. Many patients with only moderate symptoms have significant illness impact
Nickel et al <sup>60</sup>	217 IC/BPS	100	0	86% W, 7.4% Af-Am, 6.6% - Other	Retrospective analysis of RCT	BCG	QOL (SF-36), sexual functioning (SexFn)	Validated self-report	Those who responded to treatment reported improvement in sexual and sleep function. Sexual functioning and sleep disturbance (other than nocturia) strong predictors of QOL. Predicted poorer physical QOL and the strongest predictor of poorer mental QOL in sample
Nickel et al <sup>24</sup>	207 IC/BPS, 117 HC	100	0	NR	Case-control	N/A	Trauma prevalence (CTES), depression (CES-D), anxiety (STAI), catastrophizing (PCS), sexual functioning (ESSE), social support (MSPSS), QOL (SF-12)	Validated self-report	Sexual functioning impaired in sample, associated with worsened physical and mental QOL
Novi et al <sup>17</sup>	46 IC/BPS, 46 HC	100	0	82.6% W, 15.2% Af-Am, 2.2% Hisp	Case-control	N/A	Depression (PHQ-9)	Validated self-report	IC/BPS reported significantly higher rates of sexual abuse compared to controls. Abuse history associated with more pain, depression, and worse QOL. When adjusted for multiple comparisons these were no longer significant
Peters et al <sup>30</sup>	215 IC/BPS, 121 SR-IC/BPS, 464 HC	100	0	97% W, 1% Af-Am, 1% Hisp, 0.5% Asian	Case-control	N/A	Trauma prevalence	Clinical interview, non-validated self-report	Women with IC/BPS have much higher risk of depression, particularly in early stages of illness. Depression associated with worsened symptom presentation
Rabin et al <sup>28</sup>	74 IC/BPS	100	0	92.1% W, 3.9% Af-Am, 1.3% Asian, 1.3% Hisp, 1.3% Nat-Am	Observational cohort	N/A	Depression (CES-D), self-efficacy (IC-SES)	Validated self-report	Higher reported rates found by direct interview, mode of questioning may have impacted response - prevalence of abuse is already high but may be much higher due to discomfort with disclosure

Author	Sample N	Female	Male	Race	Study type	Intervention	Relevant outcomes	Measure type	Primary findings
Rapuziz-Gonzalez et al <sup>22</sup>	426 IC/BPS, 104 RC	91	9	NR	Case-control	N/A	QOL (KHQ), self-esteem (RSES), anxiety (GAS)	Validated self-report	Patients with IC/BPS had higher anxiety burden and lower QOL than RC - both diseases had significant impact on anxiety, self-esteem, QOL when compared to general population
Rothrock et al <sup>25</sup> , Rothrock et al <sup>62</sup>	64 IC/BPS; 65 IC/BPS vs 40 HC	100	0	89.1% white, 4.7% Nat-Am, 1.6% Asian, 3.1% "other"	OObservational cohort	N/A	QOL (SF-36), depression (BDI, HRSD), coping strategies (CSQ)	Validated self-report	Catastrophizing related to more severe symptomatology on all mental health measures, worse pain, and poorer social functioning. Patients had significantly greater depression levels than controls. Disease severity was not consistently related to emotional distress
Saaranen et al <sup>41</sup>	151 IC/BPS	93	7	NR	Retrospective analysis of RCT	DMSO vs BCG ( <i>n</i> = 87) and PPS vs CyA (64)	QOL (HRQoL)	Non-validated self-report	IC/BPS showed significantly impaired emotional well-being, social functioning, pain, and general health perceptions when compared to prostate cancer. There was a low response rate to questions regarding sexual functioning
Seth and Teichman <sup>31</sup>	119 IC/BPS	100	0	NR	Retrospective case-control	N/A	Abuse prevalence, sexual functioning (FSFI)	Validated self-report, clinical interview	Those with sexual abuse had different symptom presentation (increased tenderness, less urinary symptoms) and worsened sexual functioning
Tripp et al <sup>26</sup>	115 IC/BPS	100	0	94.8% White, 1.7% Af-Am, 1.7% Asian, 1.7% Hisp	Observational cohort	N/A	QOL (SF-12), depression (CESD), catastrophizing (CSQ), sexual functioning (FSFI)	Validated self-report	In IC/BPS, younger age and greater helplessness worsened mental QOL. Pain most robust predictor of physical QOL. QOL and sexual functioning not associated
Tripp et al <sup>19</sup>	190 IC/BPS, 117 HC	100	0	90% W	Case-control	N/A	Suicidality (PHQ-9/single item), depression (CESD), catastrophizing (PCS)	Validated self-report	23% of group reported SI, SI associated with more pain, depression, and catastrophizing
Tripp et al <sup>26</sup>	193 IC/BPS, 115 HC	100	0	89% W	Case-control	N/A	QOL (SF-12), depression (CESD), catastrophizing (PCS)	Validated self-report	73% of patients reported pain outside of the bladder. Those with widespread pain reported more sensory and affective pain. Urges psychosocial therapies. Psychosocial variables (catastrophizing) were significantly different than controls but not across phenotype (implications - intervention has potential to help both groups).

Author	Sample N	Female	Male	Race	Study type	Intervention	Relevant outcomes	Measure type	Primary findings
Watkins et al <sup>8</sup>	1469 IC/BPS	100	0	80.1% W, 7.7% Af-Am, 7.4% Hisp	Observational cohort	N/A	Depression (PHQ-8), anxiety (2-item screen), QOL (SF-36)	Validated self-report	Those with most widespread pain were significantly more depressed  Depression and panic associated with worsened QOL, increased symptoms and almost double the rate of not working due to Disorders likely worsen and fitness intensify each other. These women were more likely to be managed by PCP
Weissman et al <sup>21</sup>	67 IC/BPS, 79 UD, 815 FDR	84	16	88.1% W	Case-control	N/A	Anxiety disorder diagnosis (SADS-LA)	Validated structured psychiatric interview	Patients with IC/BPS show significantly increased risk of panic disorder, as well as their first-degree relatives. Suggests genetic linkage and a common 'syndrome' in some patients involving panic, bladder, and other issues such as thyroid disorders
Zaslau et al <sup>54</sup>	554 IC/BPS, 131 HC	100	0	NR	Case-control	N/A	Sexual functioning (FSFI)	Validated self-report	IC/BPS patients had significantly impacted sexual functioning in all domains. Sexual dysfunction worsened with age and degree of pain

FDR, first-degree relatives; HC, healthy control;

\* outcome data reported on IC/BPS cohort only; NR, not reported; W, white; Hisp, hispanic; Nat-Am, native American; Af-Am, African-American; RCT, randomized controlled trial; MBSR, mindfulness-based stress reduction; TAU, treatment-as-usual; UD, urologic disorders; AC, acute cystitis; RC, radiation cystitis; SR-IC/BPS, self-report suggestive of IC/BPS; DMSO, BCG, PPS, CyA, dimethyl sulfoxide, Bacille Calmette-Guerin, cyclosporine A, pentosan polysulfate sodium.



**TABLE 3**

Pooled statistics of psychosocial variables with outpatient comparison

Measure	Total N	Mean (SD)	Clinical cutoffs and interpretation
Depression			
CES-D	564	19.89 (13.12)	>16.0 cutoff for clinical depression, <sup>37</sup> >19 for clinical depression in chronic pain <sup>38</sup>
BDI-II	234	14.28 (8.51)	>14 mild depression, >20 moderate, >29 severe depression <sup>52</sup>
HADS-D	465	5.65 (4.40)	>8 detects major depression <sup>53</sup>
Anxiety, stress, and coping			
HADS-A	465	8.15 (4.85)	>8 indicates 78% chance of having generalized anxiety disorder <sup>53</sup>
PSS	659	18.61 (8.61)	>16 high health concern, >20 considered very high health concern in need of intervention <sup>54</sup>
CSQ—CAT	466	14.15 (8.60)	>20 indicates high catastrophizing where patients are at greater risk for worse health outcomes <sup>55</sup>
PCS—catastrophizing	503	22.07 (12.45)	Mean score is 20, >30 indicates clinically significant level of catastrophizing <sup>56</sup>
Quality of life			
PCS (SF-12 and SF-36)	2912	42.37 (6.67)	<47 below average physical health for U.S. population <sup>57</sup>
MCS (SF-12 and SF-36)	2912	40.80 (6.25)	<45 likely depression, <50 likely anxiety disorder, <36 indicates severe psychological impairment <sup>58</sup>
FSFI	926	16.37 (8.12)	<26 at risk of sexual dysfunction needing further evaluation <sup>59</sup>

CES-D, center for epidemiological studies of depression; BDI-II, Beck depression inventory; HADS-A/D, hospital anxiety and depression scale; PSS, perceived stress scale; CSQ, coping strategies questionnaire; PCS, pain catastrophizing scale; PCS, physical composite scale; MCS, mental composite scale; FSFI, female sexual functioning index.

**TABLE 4**

Recommended psychosocial assessment instruments for pain in urologic disease

Domain	Purpose	Instrument	Included in meta-analysis
Affective vulnerability	Depressed mood	CES-D	Yes
	Anxious mood	STAI	No
	Anger	STAXI	No
	Combination: depression/anxiety	HADS	Yes
	Combination: negative/positive affect	PANAS	No
Beliefs and attitudes	Locus of pain control	BPCQ	No
	Coping strategies	CSQ	Yes
	Self-efficacy	SEQ	No
	Catastrophizing	PCS	Yes
Environmental/social	Marital satisfaction	DAS	No
	Combination: work, family, social	WHYMPI	No

CES-D, center for epidemiological studies of depression; STAI, state trait anxiety inventory; STAXI, state trait anger expression inventory; HADS, perceived stress scale; PANAS, positive and negative affect scale; BPCQ, beliefs in pain control questionnaire; CSQ, coping strategies questionnaire; SEQ, self-efficacy questionnaire; PCS, pain catastrophizing scale; DAS, dyadic adjustment scale; WHYMPI, West Haven Yale multidimensional pain inventory.

Table adapted from “The importance of psychological assessment in chronic pain,” by D. Williams, *Current Opinion in Urology* 23, 554–560, p556.<sup>60</sup>