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Characterization of Whole Body Pain in Urologic Chronic Pelvic Pain Syndrome at Baseline – A MAPP Research Network Study

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Abstract

Purpose—We characterized the location and spatial distribution of whole body pain among patients with urologic chronic pelvic pain syndrome (UCPPS) using a body map; and compared the severity of urinary symptoms, pelvic pain, non-pelvic pain, and psychosocial health among patients with different pain patterns.

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Methods—233 women and 191 men with UCPPS enrolled in a multi-center, one-year observational study completed a battery of baseline measures, including a body map describing the location of pain during the past week. Participants were categorized as having “pelvic pain only” if they reported pain in the abdomen and pelvis only. Participants who reported pain beyond the pelvis were further divided into two sub-groups based on the number of broader body regions affected by pain: an “intermediate” group (1–2 additional regions outside the pelvis) and a “widespread pain” group (3–7 additional regions).

Results—Of the 424 enrolled patients 25% reported pelvic pain only, and 75% reported pain beyond the pelvis of which 38% reported widespread pain. Participants with greater number of pain locations had greater non-pelvic pain severity ($p<0.0001$), sleep disturbance ($p=0.035$), depression ($p=0.005$), anxiety ($p=0.011$), psychological stress ($p=0.005$), negative affect scores ($p=0.0004$), and worse quality of life ($p=0.021$). No difference in pelvic pain and urinary symptom severity were observed by increasing pain distribution.

Conclusions—Three-quarters of men and women with UCPPS reported pain outside the pelvis. Widespread pain was associated with greater severity of non-pelvic pain symptoms, poorer psychosocial health and worse quality of life, but not worse pelvic pain or urinary symptoms.

Keywords

interstitial cystitis; chronic prostatitis; clinical phenotyping; widespread pain; pelvic pain

Patients with interstitial cystitis/bladder pain syndrome (IC/BPS) or chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) commonly report non-urollogic symptoms or syndromes outside the pelvic region. There is also an association between IC/BPS, CP/CPPS and chronic overlapping pain syndromes (COPC) such as irritable bowel syndrome, fibromyalgia, and chronic fatigue syndrome^{1–3} with some studies reporting systemic (e.g., poly-symptomatic, poly-syndromic) symptom presentation.^{4, 5} It has been hypothesized that patients with localized pelvic pain might represent a different phenotype than those with more widespread systemic pain.^{6, 7} However to date, very few studies have characterized the location of body pain among men and women with IC/BPS or CP/CPPS.

Fitzgerald et al first reported that 11% of patients in the IC Database Study had “other” pain (e.g., whole body, one side, eyes, or kidney).⁸ Tripp et al used a whole-body diagram to characterize the location of pain in female IC/BPS patients.⁶ They found that as the number of body pain sites increased, patients experienced greater sensory pain, greater affective pain, higher depression scores, and diminished quality of life. Nickel et al found that female IC/BPS patients with “pelvic pain and beyond” also reported greater sleep disturbance and a higher prevalence of irritable bowel syndrome than female IC/BPS patients with “pelvic pain only.”⁹ Although these studies suggest the existence of distinct clinical subtypes in female patients, similar studies have not yet been performed in men, and no studies have examined the concept of widespreadness of body pain in either men or women. Findings in other chronic pain conditions suggest that patients with widespread pain have centralized pain characteristics.^{10–16}

Here we report the body pain mapping results of the Multi-disciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network from a large cohort of men and women with urologic chronic pelvic pain syndrome (UCPPS).¹⁷ UCPPS is an umbrella term used to describe IC/BPS in men and women, and CP/CPPS in men. To our knowledge, this is the largest body pain mapping study of UCPPS to date. Objectives of the study were to: (1) characterize the location of pain among men and women with UCPPS using a body map; (2) test the hypothesis that UCPPS patients with widespread pain have worse urinary symptoms, more severe pain, and poorer psychosocial health compared to those with more localized pain; and (3) examine if increased pain distribution is associated with longer duration of UCPPS symptoms.

METHODS

Participants

The MAPP Research Network enrolled 191 men and 233 women with UCPPS at six clinical sites across the United States. The study design, and inclusion and exclusion criteria have been described previously.¹⁸ To meet IC/BPS symptom criteria males and females had to report an unpleasant sensation of pain, pressure or discomfort, perceived to be related to the bladder and/or pelvic region associated with lower urinary tract symptoms, for most of the time during the most recent 3 months. Males who met CP/CPPS criteria had to report pain or discomfort in any of the 8 Male Genitourinary Pain Index (GUPI) domains and these symptoms had to have been present for most of the time during any 3 of the previous 6 months.¹⁹ Participants provided written informed consent following IRB-approved protocols.

Pain Assessment

The body map in Figure 1 was originally described by Margolis et al,²⁰ and used by two previous IC/BPS studies.^{6, 9} Participants were asked to check any of 45 body sites on the body map where they experienced pain in the past week. Participants reporting pain in sites 14, 15 or 16 only were considered to have “pelvic pain only”.⁷ Participants reporting pain in any of the 7 broader body regions (in color) in addition to sites 14, 15, or 16 were considered to have “pelvic pain and beyond”. Our pelvic pain only versus pelvic pain and beyond nomenclature was similar to a previous mapping study by Nickel et al.⁷ The pelvic pain and beyond group was further divided into two subgroups as shown in Figure 1: an “intermediate” group with 1–2 additional pain regions outside the pelvis, and the “widespread pain” group with 3–7 additional pain regions outside the pelvis. The threshold for “widespread pain” was operationalized to divide participants with pelvic pain and beyond into two subgroups with approximately equal numbers of patients.

Measures

The MAPP Network questionnaires have been described previously.¹⁸ Urologic measures included: Interstitial Cystitis Symptom and Problem Indexes (ICSI, ICPI), Genitourinary Pain Index (GUPI), AUA Symptom Index (AUASI), RAND Interstitial Cystitis Epidemiology (RICE) instrument to assess bladder hypersensitivity,²¹ numeric ratings of pelvic pain, frequency or urgency, MAPP Composite Pelvic Pain Score, MAPP Composite

Urinary Score, and UCPPS flare assessment.²² Non-urologic and psychosocial measures included: a numeric rating from 0–10 for non-urologic or -pelvic pain, fulfillment of standardized criteria of irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, migraine headache, or vulvodynia using the Complex Multiple Symptoms Inventory (CMSI) modules,²³ Brief Pain Inventory (BPI) for overall pain severity and pain interference, Hospital Anxiety and Depression Scale (HADS) for anxiety and depression, Positive and Negative Affect Scale (PNAS), Perceived Stress Scale (PSS) for psychological stress, Coping Strategies Questionnaires (CSQ) for pain catastrophizing, CMSI for somatic symptom burden, and PROMIS scales for fatigue and sleep disturbance. Quality of life measures included the SF-12 and GUPI. We limited our analyses to cross-sectional baseline data in this study.

Statistical Analyses

Few data were missing (<5%) for the reported outcomes. No imputations or adjustments were performed and the missing data were excluded from the analysis. Means and standard deviations were reported for continuous variables and relative frequencies for categorical variables. To test for a linear gradient effect in the 3 groups an ordinal value was assigned to each group, such that widespread pain = 2, intermediate pelvic pain and beyond = 1, and pelvic pain only = 0. The non-parametric Jonckheere-Terpstra trend test was used for the analysis of ordered progression of the measure across the 3 groups.²⁴ Analyses used SAS software 9.4(SAS Institute, Cary, NC).

RESULTS

Pain Localization Patterns and Duration of UCPPS Symptoms

Only one-quarter (25.5%) of UCPPS patients reported pelvic pain only, while three-quarters (74.5%) reported pelvic pain and beyond. The percentages of men and women in the pelvic pain only, intermediate, and widespread pain groups were shown in Table 1. Relative to men, women were more likely to experience more widespread pain (p-trend=0.039). There were no differences in the duration of UCPPS symptoms among the 3 pain groups (Table 1). Heat maps (Figure 2) show the proportion of participants who had pain in a specific location in each of the 3 pain groups.

Pelvic Pain and Urinary Symptom Severity

Men and women demonstrated no difference in the severity of pelvic pain, urinary symptom (frequency, urgency), and bladder hypersensitivity features (e.g., painful bladder filling and/or painful urgency)²¹ among the 3 pain groups (p>0.05, Table 1). Women with a greater number of pain locations were more likely to report higher GUPI pain scores (p=0.033) and symptom flare at the time of visit (p=0.012).

Non-Pelvic Pain Severity and Chronic Overlapping Pain Conditions (COPC)

Men and women with a greater number of pain locations were more likely to report higher levels of non-pelvic pain severity (0–10 numeric ratings), and symptoms consistent with irritable bowel syndrome, fibromyalgia, and migraine headache (p<0.05, see Table 2). Women with a greater number of pain locations were also more likely to report higher pain

interference scores (BPI), and symptoms consistent with chronic fatigue syndrome and multiple (≥ 2) COPC.

Psychosocial Health and Quality of Life

Men and women with greater number of pain locations had greater sleep disturbance (PROMIS), depression, anxiety (HADS), psychological stress (PSS), somatic symptom burden (CMSI), and negative affect scores (PANAS) ($p < 0.05$, Table 2). Women with a greater number of pain locations were also more likely to report pain catastrophizing (CSQ) and fatigue (PROMIS), and a decrease in positive affect (PANAS). While the more general physical health and mental health domains of the SF-12 deteriorated across the gradient of increasing pain distribution, no trend was noted for urinary specific quality of life on the GUPI in either men or women.

Comparison of the Two Subgroups with Pelvic Pain and Beyond

Individuals commonly report pain in parts of their bodies from time to time (e.g., >40% of participants reported back pain or headache). To determine whether patients in the “intermediate” group with a limited distribution of pain outside the pelvis had a different presentation than those with “widespread pain”, we performed additional comparisons of the two subgroups (Table 3). Men and women with widespread pain reported more severe non-pelvic pain, and were more likely to have fibromyalgia, depression, higher psychological stress, higher somatic symptom burden, and worse physical health (SF-12) than men and women in the intermediate group. Men with widespread pain were additionally more likely to have migraine headache, anxiety, pain catastrophizing, more negative affect and less positive affect; while women with widespread pain were additionally more likely to have irritable bowel syndrome, chronic fatigue syndrome, multiple (≥ 2) COPC, sleep disturbance, fatigue, and worse mental health (SF-12) than their respective intermediate group. In both sexes, there was no difference in pelvic pain and urinary symptom severity between the two subgroups.

DISCUSSION

Despite being enrolled because of their UCPPS, most patients in this large multi-site study (75%) reported additional pain outside the pelvis/abdomen, and 38% reported a widespread pain distribution. In both men and women, increasing anatomic pain distribution was associated with greater non-pelvic pain severity, a higher prevalence of chronic overlapping pain conditions, poorer psychosocial health, and worse quality of life. In contrast, there was no difference in the severity of pelvic pain and urinary symptoms among the three pain subgroups. UCPPS patients with widespread pain appeared to be distinct from patients with more limited distribution of pain outside the pelvis (the intermediate group) as shown in Table 3.

Our overall findings were consistent with the previous studies: women with IC/BPS and systemic pain were more likely to have more severe overall pain, other pain syndromes, and worse quality of life than women who reported pelvic pain only.^{6, 9} Previous body pain

mapping studies did not include men.^{6, 9} Here we studied a large cohort of men with IC/BPS or CP/CPPS, and demonstrated many similar findings in both sexes.

Body pain mapping may confer important information suggesting discrete UCPPS patient subgroups. Pain involving several body regions is likely to represent systemic pathophysiology characterized by centralized pain characteristics (e.g., driven by central sensitization and/or neuro-immune processes). Although the operational definitions of widespread pain varied between studies, literature from other chronic pain conditions suggests that the subgroup of patients with widespread pain may have more severe pain, decreased pain thresholds, and a centralized pain phenotype.^{10–16} For instance, patients with temporomandibular disorders and widespread pain had reduced pressure pain thresholds in both cranial and extra-cranial regions compared to similar patients with more localized pain.¹⁰ Patients with epicondylitis and multidisciplinary pain clinic patients with widespread pain also had lower pressure pain thresholds or increased central sensitization than similar patients with localized pain.^{11, 12} Here we have shown that a substantial proportion of UCPPS patients have widespread pain, and those with widespread pain have more intense whole body pain. Ongoing MAPP neuroimaging studies also suggest that UCPPS patients with widespread pain have altered brain structure and function.^{25, 26} In future studies we shall examine the pain thresholds and quantitative sensory testing data on these patients.

Assessing the severity of pelvic pain, urinary symptoms (frequency, urgency), or bladder hypersensitivity (e.g., painful bladder filling, painful urgency)²¹ alone cannot distinguish between the pelvic pain only group and the widespread pain group. Instead, the body map might identify patients who may have a more centralized pain syndrome possibly related to central sensitization. The body pain map may also be used to screen patients who may benefit from clinical evaluation for other chronic overlapping pain conditions (COPC). For example, among women with UCPPS in the widespread pain subgroup, 48% had irritable bowel syndrome, 26% had fibromyalgia, 31% had chronic fatigue syndrome, and 42% had migraine headaches. Among men with UCPPS in the widespread pain subgroup, these percentages were 34%, 13%, 5% and 24%, respectively. Women with widespread pain were more likely to have multiple (≥ 2) COPC. Despite widespreadness of pain being a cardinal component of fibromyalgia, it should be noted that relatively few UCPPS patients with widespread pain met the criteria for fibromyalgia (only 13% of men and 26% of women).²⁷ The difference being that besides widespread pain, fibromyalgia also requires other symptoms (e.g., fatigue, somatic symptoms). The body pain map might also be used to screen for patients with high psychosocial burden (depression, anxiety, psychological stress, negative affect, pain catastrophizing). The body pain map (Figure 1) is simple to use, and can be included in the evaluation of IC/BPS and CP/CPPS.

Clinicians should consider the use of clinical phenotyping so they may tailor treatment to patients with UCPPS. It is possible that body pain mapping may be useful for categorization of the heterogeneous UCPPS population, and may inform more rational management strategies. For example, one might hypothesize that patients with bladder hypersensitivity features²¹ and localized “pelvic pain only” may be more likely to benefit from bladder-centric treatments (e.g., intravesical instillation, or pentosanpolysulfate). One might also hypothesize that UCPPS patient subpopulations with widespread pain might be less likely to

benefit from bladder/pelvic-directed treatments alone and might require systemic therapies for centrally mediated mechanisms (e.g., using tricyclic antidepressants, gabapentinoids, SNRI, or multidisciplinary pain management). Because many patients with widespread pain report increased psychosocial difficulties, they may also benefit from multi-modal and multi-disciplinary therapies. Using a “one size fits all” approach to treat IC/BPS or CP/CPPS patients without regards for their discrete clinical characteristics (e.g., localized versus systemic pain) and pathogenesis may lead to treatment failures. In part, these hypotheses may explain why most prior randomized controlled trials failed to demonstrate clinically significant benefits of treating the entire UCPPS population using similar therapies. This is an important area for future translational studies because currently there is no high level evidence (randomized controlled trials) supporting this personalized approach to managing UCPPS.^{28, 29}

There are potential weakness in this study: (1) we did not collect data on tobacco abuse, musculoskeletal trauma, myofascial pain, or medical conditions (e.g. osteoarthritis, rheumatoid arthritis) that may influence the distribution of pain; (2) It has been hypothesized that UCPPS patients might progress over time from localized pain to loco-regional pain to systemic pain (e.g. central sensitization).^{1, 4, 30} Our data as well as those from Nickel et al⁹ did not show a correlation between the duration of UCPPS symptoms and increased body pain distribution. However we cannot infer longitudinal trend from these cross-sectional data (e.g., there are risks of recall bias), longitudinal studies are needed to determine if there is temporal progression from one body pain pattern to another over time.

CONCLUSION

Three-quarters of men and women with UCPPS (IC/BPS or CP/CPPS) reported pain outside the pelvis. Widespread pain was associated with greater severity of non-pelvic pain symptoms, poorer psychosocial health and worse quality of life, but not worse pelvic pain or urinary symptoms.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Assignment of the pain groups: pelvic pain only (0 region), an intermediate group with pain beyond pelvis (1–2 regions), and widespread pain (3–7 regions).

Figure 2.

The numbers on the heat maps refer to the proportion of participants, within of the 3 defined subgroups, who experienced pain at that site.

Table 1

Demographics, comparison of pelvic pain and urinary symptom severity.

	Men (n = 191)				Women (n = 233)			
	Pelvic Pain Only (0 region)	Intermediate (1–2 regions)	Widespread Pain (3–7 regions)	p value (3 group trend)	Pelvic Pain Only (0 region)	Intermediate (1–2 regions)	Widespread Pain (3–7 regions)	p value (3-group trend)
No. of participants, n (%)	57 (29.8)	72 (37.7)	62 (32.5)		51 (21.8)	88 (37.7)	94 (40.3)	
Demographics:								
Age, mean years (SD)	48.4 (16.1)	46.7 (14.9)	45.5 (15.2)	0.311	40.4 (13.4)	40.3 (14.9)	40.9 (14.5)	0.809
Race: White, n (%)	53 (93)	63 (87.5)	55 (88.7)	0.465	47 (92.2)	80 (90.9)	85 (90.4)	0.745
Ethnicity: Hispanic, n (%)	1 (1.8)	3 (4.2)	6 (9.7)	0.051	3 (5.9)	10 (11.4)	5 (5.3)	0.584
Duration of symptoms, mean years (SD)	8.7 (11.9)	7 (9.3)	7.9 (11.2)	0.323	8.6 (9.5)	6.5 (7.8)	11.9 (12.6)	0.100
Duration of symptoms <1 years, n (%)	5 (8.8)	4 (5.6)	9 (14.5)	0.235	3 (5.9)	6 (6.8)	8 (8.5)	0.612
Age at diagnosis of IC/BPS, mean years (SD)	39.2 (12.9)	40.4 (13.1)	39.9 (13.1)	0.795	20	41.8 (13.1)	31.1 (12.1)	0.547
Age at diagnosis of CP/CPSP, mean years (SD)	49.2 (14.4)	44.6 (16.5)	39.8 (13.2)	0.12	NA	NA	NA	NA
Medication Class:								
Central acting (e.g., pregabalin, tricyclics)	26 (45.6)	29 (40.3)	29 (46.8)	0.875	23 (45.1)	36 (40.9)	43 (45.7)	0.799
Peripheral acting (e.g., pentosan polysulfate)	12 (21.1)	6 (8.3)	5 (8.1)	0.034	8 (15.7)	25 (28.4)	19 (20.2)	0.891
Opioids	4 (7)	6 (8.3)	6 (9.7)	0.602	2 (3.9)	11 (12.5)	14 (14.9)	0.071
None	15 (26.3)	31 (43.1)	22 (35.5)	0.328	18 (35.3)	16 (18.2)	18 (19.1)	0.067
Urologic and Pelvic Pain Severity:								
Pelvic pain (numeric ratings, 0–10)	5.1 (2.2)	4.5 (2.3)	5 (2.2)	0.844	5.1 (2)	5.1 (2.1)	5.5 (2.3)	0.243
Overall urologic or pelvic pain symptoms (0–10)	5.1 (2.2)	4.7 (2.5)	5.1 (2.3)	0.896	5 (2.2)	5.2 (2.3)	5.7 (2.4)	0.061
GUPI Pain score (0–23)	12.2 (3.7)	12 (4.5)	12.4 (4.5)	0.85	12.3 (4.1)	12.3 (4.7)	13.7 (4.7)	0.033*
MAPP Composite Pain Score (0–28) ^a	13.5 (4.8)	14.2 (5.6)	14.4 (5.6)	0.409	15.2 (5.1)	15.1 (5.8)	16.8 (5.7)	0.059

	Men (n = 191)				Women (n = 233)			
	Pelvic Pain Only (0 region)	Intermediate (1–2 regions)	Widespread Pain (3–7 regions)	p value (3 group trend)	Pelvic Pain Only (0 region)	Intermediate (1–2 regions)	Widespread Pain (3–7 regions)	p value (3-group trend)
Urinary Symptom Severity:								
Frequency (numeric ratings, 0–10)	5 (2.7)	4.4 (2.5)	4.7 (2.6)	0.692	5.1 (2.3)	5.4 (2.6)	5.5 (2.6)	0.403
Urgency (numeric ratings, 0–10)	4.8 (2.7)	4.4 (2.6)	4.7 (2.5)	0.856	4.9 (2.7)	4.9 (2.6)	5.4 (2.5)	0.157
GUPI Urinary score (0–10)	5 (3.1)	4.2 (2.8)	5.1 (2.7)	0.68	5.6 (2.8)	5.5 (3)	6 (3.1)	0.285
MAPP Composite Urinary Score (0–25) ^a	12.6 (6.9)	10.3 (5.9)	11.4 (5.7)	0.483	13.3 (5.7)	13 (6)	14.3 (6.4)	0.204
AUA Symptom Index (0–35)	14.7 (8.5)	12.9 (7.3)	14.4 (9)	0.632	15.6 (6.9)	15.7 (8.9)	18.2 (9)	0.075
Composite Scores:								
IC symptom index (0–20)	8.9 (5.1)	8.3 (4.6)	8.3 (4.4)	0.665	10.5 (4.4)	10.3 (4.4)	11.3 (4.6)	0.172
IC problem index (0–16)	7.8 (4.8)	6.9 (4.4)	7.4 (4.4)	0.72	9.2 (3.9)	9.1 (4)	10 (4.1)	0.132
GUPI Total score (0–45)	24.9 (7.2)	23.5 (8.7)	25.6 (8.2)	0.739	25.6 (8.5)	25.5 (9.3)	27.8 (8.7)	0.119
Bladder hypersensitivity (RICE): Both, Neither, Either ^b	B: 24.6% E: 33.3% N: 42.1%	B: 20.8% E: 41.7% N: 37.5%	B: 29.0% E: 27.4% N: 43.6%	0.875	B: 24.6% E: 33.3% N: 42.1%	B: 20.8% E: 41.7% N: 37.5%	B: 29.0% E: 27.4% N: 43.6%	0.0856
Flare occurring at baseline visit (yes/no), n (%)	10 (17.5)	18 (25)	18 (29)	0.146	10 (19.6)	27 (30.7)	37 (39.4)	0.012*

Trend p-values were obtained from the non-parametric Jonckheere-Terpstra Test.

^aGriffith et al (2016).

^bLai et al (2015).

Table 2

Comparison of non-pelvic pain severity, psychosocial, and quality of life measures.

	Men (n = 191)				Women (n = 233)			
	Pelvic Pain Only (0 region)	Pelvic Pain and Beyond		p value (3 group trend)	Pelvic Pain Only (0 region)	Pelvic Pain and Beyond		p value (3 group trend)
		Intermediate (1–2 regions)	Widespread Pain (3–7 regions)			Intermediate (1–2 regions)	Widespread Pain (3–7 regions)	
Non-Urologic or Pelvic Pain Intensity:								
Overall non-pelvic pain (numeric ratings, 0–10)	1.3 (1.6)	2.6 (2.5)	4.2 (2.5)	<.0001*	1.5 (2)	3.4 (2.7)	5.1 (2.4)	<.0001*
Brief Pain Inventory (BPI) whole body pain:								
Pain severity, BPI (0–10)	2.9 (2.1)	2.8 (2.4)	4.1 (2.8)	0.029*	3.3 (2.5)	4 (2.8)	4.9 (2.9)	0.001*
Pain interference, BPI (0–10)	3.5 (1.9)	3.7 (2)	4.1 (2.1)	0.131	3.7 (1.8)	4 (1.8)	4.8 (1.9)	<.0001*
COPC (Chronic Overlapping Pain Conditions), n (%)								
Irritable bowel syndrome	9 (15.8)	21 (29.2)	21 (33.9)	0.028*	5 (9.8)	26 (29.5)	45 (47.9)	<.0001*
Fibromyalgia	0 (0)	1 (1.4)	8 (12.9)	0.001*	3 (5.9)	2 (2.3)	24 (25.5)	<.0001*
Chronic fatigue syndrome	1 (1.8)	5 (6.9)	3 (4.8)	0.454	3 (5.9)	8 (9.1)	29 (30.9)	<.0001*
Migraine Headache	3 (5.3)	7 (9.7)	15 (24.2)	0.002*	4 (7.8)	28 (31.8)	39 (41.5)	<.0001*
Vulvodynia	NA	NA	NA	NA	9 (17.6)	16 (18.2)	19 (20.2)	0.675
Multiple (2) COPC?	1 (1.8)	3 (4.2)	4 (6.5)	0.203	3 (5.9)	4 (4.5)	26 (27.7)	<.0001*
Quality of Life:								
SF-12 Physical Health (0–100)	51.1 (8.7)	51.6 (8.4)	47.3 (9.5)	0.021*	51.9 (6.9)	45.8 (10)	41 (11.2)	<.0001*
SF-12 Mental Health (0–100)	47.8 (9.1)	44.4 (11.1)	41 (11.2)	0.001*	46.2 (8.7)	44.9 (10.5)	40.7 (10.3)	0.001*
GUPI urinary-specific quality of life (0–12)	7.6 (2.4)	7.1 (3.1)	8.1 (2.7)	0.34	7.7 (2.9)	7.7 (3)	8 (2.9)	0.471
Psychosocial Health:								
Depression, HADS (0–21)	4.7 (3.5)	4.9 (4.3)	6.8 (4.1)	0.005*	3.6 (3)	5 (3.9)	6.5 (4.8)	<.0001*
Anxiety, HADS (0–21)	6.5 (4)	7 (4.6)	8.8 (4)	0.004*	6.2 (3.9)	8 (4.4)	8.7 (5.2)	0.011*
Positive affect, PANAS (5–50)	30.6 (6.8)	32 (7.3)	28.7 (7.6)	0.16	32.2 (7.8)	29.5 (7.3)	27.4 (8)	0.001*
Negative affect, PANAS (5–50)	19.2 (7.1)	19.8 (7.7)	23 (7.3)	0.004*	18.8 (7.1)	21.1 (8.1)	23.5 (9)	0.001*

	Men (n = 191)				Women (n = 233)			
	Pelvic Pain and Beyond				Pelvic Pain and Beyond			
	Pelvic Pain Only (0 region)	Intermediate (1–2 regions)	Widespread Pain (3–7 regions)	p value (3 group trend)	Pelvic Pain Only (0 region)	Intermediate (1–2 regions)	Widespread Pain (3–7 regions)	p value (3 group trend)
Stress, PSS (0–40)	13.8 (7.2)	14.7 (7)	17.6 (6.9)	0.005*	13.7 (6.7)	16.5 (7.7)	20 (9)	<.0001*
Pain Catastrophizing, CSQ (0–36)	10 (8)	9.5 (8.2)	12.6 (9.2)	0.119	12.4 (7.9)	13.7 (8.2)	15.5 (9.5)	0.042*
Somatic burden last year, CMSI (0–39, Males; 0–41, Females)	6.9 (3.6)	8.4 (4.5)	11.9 (6.5)	< .0001*	8.3 (5.4)	11.9 (7)	17.8 (9.2)	< .0001*
Somatic burden lifetime, CMSI (0–39, Males; 0–41, Females)	9.3 (10.2)	10.9 (10)	8.9 (8.5)	0.873	8 (8.4)	10.3 (9.5)	11.7 (8.4)	0.003*
Fatigue, PROMIS T Score (29.4–83.2)	51.9 (6.2)	51.7 (7.2)	53.9 (6.5)	0.08	51.7 (6.4)	54.9 (6.8)	57.9 (7.1)	< .0001*
Sleep disturbance, PROMIS T Score (28.9–76.5)	51.1 (7.1)	51.9 (9.4)	55.1 (9.3)	0.035*	52.3 (8.8)	54.9 (9)	58.7 (9.2)	< .0001*

Trend p-values were obtained from the non-parametric Jonckheere-Terpstra Test.

Table 3

Intermediate versus widespread pain subgroup comparison.

	Men (n=134)	Women (n=182)
Comparison of the 2 subgroups with Pelvic Pain and Beyond	p value ^{***} Intermediate (1–2) vs. Widespread Pain (3–7)	p value ^{***} Intermediate (1–2) vs. Widespread Pain (3–7)
Urologic and Pelvic Pain Severity:		
Pelvic pain (numeric ratings, 0–10)	0.192	0.254
Overall urologic or pelvic pain symptoms (0–10)	0.394	0.12
GUPI Pain score (0–23)	0.616	0.052
MAPP Composite Pain Score (0–28) ^a	0.896	0.073
Urinary Symptom Severity:		
Frequency (numeric ratings, 0–10)	0.558	0.403
Urgency (numeric ratings, 0–10)	0.621	0.157
GUPI Urinary score (0–10)	0.069	0.285
MAPP Composite Urinary Score (0–25) ^a	0.208	0.204
AUA Symptom Index (0–35)	0.501	0.075
Composite Scores:		
IC symptom index (0–20)	0.802	0.103
IC problem index (0–16)	0.519	0.124
GUPI Total score (0–45)	0.242	0.125
Bladder hypersensitivity (RICE): Both, Either, Neither ^b	0.971	0.256
Flare occurring at baseline visit (yes/no), n (%)	0.56	0.182
Non-Urologic Pain:		
Overall non-pelvic pain (numeric rating, 0–10)	<.0001*	<.0001*
Brief Pain Inventory (BPI) whole body pain:		
Pain severity, BPI (0–10)	0.006*	0.036*
Pain interference, BPI (0–10)	0.324	0.003*
COPC (Chronic Overlapping Pain Conditions): N (%)		
Irritable bowel syndrome	0.558	0.011*
Fibromyalgia	0.008*	<.0001*

	Men (n=134)	Women (n=182)
Comparison of the 2 subgroups with Pelvic Pain and Beyond	p value ^{**} Intermediate (1–2) vs. Widespread Pain (3–7)	p value ^{**} Intermediate (1–2) vs. Widespread Pain (3–7)
Chronic fatigue syndrome	0.608	<.0001*
Migraine Headache	0.024*	0.176
Vulvodynia	NA	0.729
Multiple (2) NUAS?	0.553	<.0001*
Quality of Life:		
SF-12 Physical Health (0–100)	0.006*	0.005*
SF-12 Mental Health (0–100)	0.071	0.017*
GUPI urinary quality of life score (0–12)	0.092	0.463
Psychosocial Health:		
Depression, HADS (0–21)	0.003*	0.036*
Anxiety, HADS (0–21)	0.007*	0.407
Positive affect, PANAS (5–50)	0.008*	0.104
Negative affect, PANAS (5–50)	0.006*	0.058
Stress, PSS (0–40)	0.016*	0.01*
Pain Catastrophizing, CSQ (0–36)	0.043*	0.196
Somatic burden last year, CMSI (0–39, Males; 0–41, Females)	0.003*	<.0001*
Somatic burden lifetime, CMSI (0–39, Males; 0–41, Females)	0.291	0.096
Fatigue, PROMIS T Score (29.4–83.2)	0.09	0.01*
Sleep disturbance, PROMIS T Score (28.9–76.5)	0.063	0.008*

**

The numeric values have already presented in Tables 1 & 2.

To examine if there were differences between the intermediate and widespread pain groups, a Chi-square test was used for binary variables of interest while a Wilcoxon-Mann-Whitney test was used for continuous or ordinal variables of interest with a 2-sided significance level of alpha = 0.05.

^aGriffith et al (2016).

^bLai et al (2015).