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Comorbidities in a Nationwide, Heterogenous Population of Veterans with Interstitial Cystitis/Bladder Pain Syndrome

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Abstract

OBJECTIVE—To examine the prevalence of comorbid conditions in a nationwide population of men and women with IC/BPS utilizing a more heterogeneous sample than most studies to date.

METHODS—Using the Veterans Affairs Informatics and Computing Infrastructure, we identified random samples of male and female patients with and without an ICD-9/ICD-10 diagnosis of IC/BPS. Presence of comorbidities (NUAS [chronic fatigue syndrome, fibromyalgia, irritable bowel syndrome, migraines], back pain, diabetes, and smoking) and psychosocial factors (alcohol abuse, post-traumatic stress disorder, sexual trauma, and history of depression) were determined using ICD-9 and ICD-IO codes. Associations between these variables and IC/BPS status were evaluated while adjusting for the potential confounding impact of race/ethnicity, age, and gender.

RESULTS—Data was analyzed from 872 IC/BPS patients (355 [41%] men, 517 [59%] women) and 558 non-IC/BPS patients (291 [52%] men, 267 [48%] women). IC/BPS patients were more likely than non-IC/BPS patients to have a greater number of comorbidities (2.72+/−1.77 vs 1.73+/−1.30, $P < 0.001$), experience one or more NUAS (chronic fatigue syndrome, fibromyalgia, irritable bowel syndrome, and migraines) (45% [388/872] vs. 18% [101/558]; $P < 0.001$) and had a higher prevalence of at least one psychosocial factor (61 % [529/872] v. 46% [256/558]; $P < 0.001$). Differences in the frequencies of comorbidities between patients with and without IC/BPS were more pronounced in female patients.

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SUPPLEMENTARY MATERIALS

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CONCLUSION—These findings validate the findings of previous comorbidity studies of IC/BPS in a more diverse population.

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic pelvic pain condition defined as bladder-centric pain in the absence of infection. The Society for Urodynamics and Female Urology (SUFU) stipulates that these symptoms must be present for at least six weeks, and other related conditions excluded, before reaching an IC/BPS diagnosis[1]. Conditions that present similarly and sometimes concurrently with IC/BPS, and should there-fore be taken into consideration when evaluating a potential IC/BPS patient include: urinary tract infection (UTI), overactive bladder, and other pelvic pain conditions such as endometriosis and chronic prostatitis. Urine cultures, cystoscopy, and urodynamic results are often variable leaving providers without an objective test to directly and definitively diagnose IC/BPS.[2] Consequentially, the diagnosis is subjective and relies heavily on the clinician's assessment of the patient's history and symptoms. Obtaining a fuller understanding of the comorbidities associated with IC/BPS may aid clinicians in achieving a more comprehensive approach to treatment.

IC/BPS patients frequently present with other non-urological associated somatic syndromes (NUAS) as well as psychosocial comorbidities.[3–5] The Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) network characterized NUAS as "non-urologic syndromes that co-occur with urologic chronic pelvic pain syndrome (UCPPS) at a rate greater than the general population" and classified fibromyalgia, irritable bowel syndrome (IBS), chronic fatigue syndrome, migraines, among other conditions in this category.[6] The MAPP network also recognized the association between chronic pelvic pain syndromes and psychosocial factors such as anxiety and depression.[4] The breadth and strength of the association between these comorbidities and IC/BPS varies between studies and is yet to be fully elucidated.[7,8] Furthermore, the potential association between IC/BPS and health behaviors such as smoking history and diabetes, has been minimally explored.

To address these gaps, we investigated the relationship between NUAS, psychosocial factors, and behavior/life-style among patients with and without IC/BPS. Utilizing a dataset of ICD-9/ICD-10 codes for comorbidities we were able to subcategorize the existing comorbidity data into the afformentioned groups. By determining the prevalence of relevant comorbidities among IC/BPS patients in a heterogeneous population of men and women, we aim to add clarity to the existing literature and introduce novel information regarding minimally studied comorbidities, such as PTSD. Utilizing a cohort of veterans nationwide provides us with a more diverse and representative sample than most populations studied to date. We hypothesized that patients with an IC/BPS diagnosis would be more likely to have a diagnosis of a NUAS or a psychosocial disorder, overall be more health-conscious and therefore less likely to engage in unhealthy behaviors such as smoking or alcohol abuse than non-IC/BPS patients.

MATERIALS AND METHODS

Data Source/Ascertainment of Study Cohort

We utilized the largest nationally integrated health care system, the Veterans Health Administration (VHA), to develop nationally representative cohorts of subjects with and without IC/BPS. All data from all VHA sites are collated into a common electronic medical record called VA Informatics and Computing Infrastructure (VINCI). After obtaining IRB approval, on January 4, 2017 we queried VINCI to identify 164,845 living patients with an ICD-9/1CD-10 diagnosis of IC/BPS (595.1/N30.10) between 1999 and 2016 who had at least two encounters where a clinical history was recorded in the VHA healthcare system. We sought a gender balanced sample, taking into consideration the smaller female population in the VHA and the potential for underdiagnosis of IC/BPS in males. We randomly selected patients at a 3:2 ratio with and without an ICD-9/ICD-10 diagnosis of IC/BPS to perform an in-depth chart review to abstract demographic information, smoking history, and screen for exclusion criteria. While we had randomly selected 1,600 IC/BPS patients and 1,093 non-IC/BPS patients, at the time of this analysis, chart reviews had been completed for 1,352 IC/BPS patients and 813 non-IC/BPS patients.

IC/BPS patients were excluded if they met any of the following criteria: any cancer except non-melanoma skin cancer, HIV positive status, history of cystectomy, transgender, dementia/hallucinations, neurogenic voiding dysfunction, ileovesicostomy/urostomy, end stage renal disease, or ureteral stent placement around time of diagnosis. Non-IC/BPS patients were excluded if they met any of the IC/BPS exclusion criteria, as well as any of the following conditions: chronic prostatitis, dyspareunia, vaginismus, vulvodynia, vulvar vestibulitis, or ≥ 2 UTIs in the past year. Any subject from the non-IC/BPS group that was found to have IC based on manual chart review was excluded in total as there was no associated ICD-9/ICD-10 code and could introduce selection bias. After individual chart review, 480 patients from the IC/BPS cohort and 255 from the non-IC/BPS cohort were excluded. This resulted in a final sample of 872 IC/BPS patients and 558 non-IC/BPS patients (Fig.W 1).

We used VINCI to search for a diagnosis of 10 comorbidities in veterans' medical records based on ICD-9/ICD-10 codes (Appendix 1). The ICD-IO codes we selected for IC/BPS, back pain, chronic fatigue syndrome, fibromyalgia, IBS, and migraines have since been validated by a 2019 study that identified ICD10 codes optimal for standardizing studies on chronic overlapping pain conditions.[9] We classified chronic fatigue syndrome, irritable bowel syndrome, fibromyalgia and migraines, as NUAS based on the MAPP definition and alcohol abuse, post-traumatic stress disorder, sexual trauma, and history of depression as psychosocial factors.[6] Additional comorbidities that did not fall into either category included back pain and diabetes.

As our cohort included the period of time when the transition from ICD-9 to ICD-IO procedure codes occurred (October 1,2015), there was the possibility that certain comorbidities would be captured differently before and after the transition. For example, there was no specific ICD-9 code for Fibromyalgia (Appendix 1). Although patients would theoretically have their diagnosis codes updated, this was contingent on the fact that they

had regular care at a VA facility after the ICD-IO transition date. To address this potential limitation, we performed a sensitivity analysis where we divided our cohort into two groups (those who had their IC/BPS diagnosis before or after the transition to ICD-IO coding on October 1, 2015). We then compared the rates of the comorbidities of interest between these two groups to ensure that there was no significant difference in the rates of these conditions after the transition to ICD-IO coding (Appendix 2).

Statistical Analysis

Differences between groups were initially tested with a Student's T-test for continuous measures and Chi-square test for categorical data. Differences in the number or prevalence of specific comorbidities were tested with multivariable Poisson or logistic regression and adjusted for race, age, and gender in all modeling. Additional regression models were performed to include the interaction of gender with IC/BPS disease status. Exact methods were used where counts were less than 5. All testing was performed at the two-tailed 0.05 significance level with post-hoc Tukey testing to adjust for multiple comparisons. Data are presented as mean +/− standard deviation (SD) or counts and percentages. Odds ratios are presented with 95% confidence intervals (CI). Analysis was performed using SAS Enterprise Guide v7.1 software.

RESULTS

The final sample consisted of 41% (355/872) male and 59% (517/872) female IC/BPS patients and 52% (291/558) male and 48% (267/558) female non-IC/BPS patients (Table 1, $P < 0.001$). IC/BPS patients were significantly older at the time of analysis (57.1 vs. 53.9 years, $P<0.001$). Subjects with IC/BPS were more likely to be white ($P < 0.001$) and less likely to be African American ($P = 0.005$).

On average, IC/BPS patients had 2.7 comorbidities per person compared with non-IC/BPS patients who had 1.7, which was significant even after adjusting for age and other demographic characteristics (Table 1, $P < 0.001$). 92% of IC/BPS had at least one of the comorbidities compared to 84% of non-IC/BPS cases (OR = 2.2; 95% Cl: 1.5, 3.1; $P<0.001$). The most frequently reported comorbidity in both groups was back pain, although IC/BPS cases were significantly more likely to report back pain than non-IC/BPS (OR = 2.2; 95% Cl: 1.7, 2.8; $P < 0.001$). The odds of experiencing a NUAS was higher among IC/BPS patients vs. non-IC/BPS patients in both male and female cohorts (OR = 3.5; 95%C1: 2.7, 4.6; p<0.001). IBS was the most significant contributor in the difference between IC/BPS and non-IC/BPS cases (OR = 4.1; 95% Cl: 2.8, 6.0; $p<0.001$). The odds of psychosocial factors was higher in the IC/BPS cohort (OR = 1.9; 95% Cl: 1.5, 2.4; P<0.001). Notably, the odds of a PTSD diagnosis was higher among IC/BPS patients than non-IC/BPS patients (OR = 2.0; 95%C1: 1.5, 2.5; $P < 0.001$). Health behaviors including alcohol abuse, smoking history, and diabetes were not significantly different between IC/ BPS and non-IC/BPS patients ($P = 0.083$, $P = 0.067$, $P = 0.626$ respectively).

Male patients were older than female patients at time of analysis in both cohorts (Table 2). On average, males were 16 years older than females ($P < 0.001$) in the IC/BPS cohort and 13 years older in the non-IC/BPS cohort ($P<0.001$). The odds of having at least 1 comorbidity

was higher for female IC/BPS patients vs. male IC/BPS patients (OR = 2.6; 95% Cl: 1.2, 5.4; P= 0.005). Female IC/BPS patients tended to have more comorbidity diagnoses than male IC/BPS patients (3.2 v. 2.1, P< 0.001). The odds of having a NUAS was higher for female IC/BPS patients vs. male IC/BPS patients (OR = 3.5; 95%C1: 2.3, 5.4; P<0.001). Female IC/BPS patients had greater odds of psychosocial factors than male IC/BPS patients (OR = 1.9; 95% Cl: 1.3, 2.8; P < 0.001). The female IC/BPS patients had a significantly higher prevalence of sexual trauma compared to the female non-IC/BPS patients (13% vs. 6%, P < 0.05), while none of the male IC/BPS reported sexual trauma.

Sensitivity analysis comparing the rates of comorbidities of interest before and after the transition to ICD-IO coding revealed no significant difference between the two groups (Appendix 2).

DISCUSSION

Using a nationwide cohort of men and women, our work revealed many significant findings, the most significant of which was the strong association between IC/BPS and both NUAS and psychosocial factors. Patients with an IC/BPS diagnosis were more than twice as likely to have a NUAS than non-IC/BPS patients in male and female cohorts. There was an increased prevalence of all four NUAS in the IC/BPS cohort. Moreover, we found IC/BPS patients had a greater likelihood of having at least one psychosocial comorbidity. Female IC/BPS patients had a greater prevalence of all psychosocial factors compared to male IC/BPS patients. These results indicate a strong correlation between these broader categories of comorbidities and IC/BPS, although causation cannot be determined from our study.

The MAPP Network has previously studied NUAS in patients with urologic chronic pelvic pain syndrome (UCPPS), which includes IC/BPS and chronic prostatitis/chronic pelvic pain syndrome. Their study examined chronic fatigue syndrome, fibromyalgia, and IBS and discovered a 38% prevalence of at least one of these NUAS in their UCPPS patients.[3] We included migraines in our NUAS analysis because the MAPP Network has acknowledged migraines as a NUAS and we had access to data for this ICD-9/ICD-10 code.[6] In doing so, we found a slightly higher prevalence of 45% (388/872); however, for thoroughness we also excluded migraines and re-evaluated the data which resulted in a 42% prevalence, even closer to that found in the MAPP. These findings uphold the hypothesized association between IC/BPS and NUAS comorbidities. In regards to the NUAS results, we were specifically surprised by fibromyalgia's prevalence, which was approximately three-fold in females and two-fold in males with IC/BPS. We find this notable because of fibromyalgia's relative rarity in men.[10] For example, a 2012 study in Minnesota found an age-adjusted prevalence of 0.15% for men with an ICD-9 diagnosis of fibromyalgia.[11] Overall, clinicians' awareness of the increased prevalence of NUAS comorbidities and their impact on IC/BPS may aid in treatment in that patients suffering from NUAS in addition to IC/BPS may benefit from an interdisciplinary approach to care.

Researchers have suspected a psychosocial component to IC/BPS for some time. Several previous studies have confirmed an association with depression although estimates vary widely.[12, 13] A 2018-meta analysis evaluated 16 studies on depression in IC/BPS patients

and revealed prevalence rates ranging from 16–70%. [7] Our data support an association between depression and IC/BPS and adds clarity by demonstrating a 46% (398/872) prevalence compared to 29% (161/558) in the non-IC/BPS cohort. The relationship between IC/BPS and PTSD is also understudied. In one of the few studies examining this potential association, McKernan et al. assessed a small IC/ BPS cohort (n=64) for PTSD as well as childhood trauma, sexual abuse, and emotional distress utilizing a series of validated surveys.[7] Their results yielded 42% of IC/BPS patients meeting provisional criteria for PTSD, a five-fold increase from the general population. [7, 14] Our study population was much larger (n = 872) and we relied on the PTSD diagnosis code in the medical record. Interestingly, despite these differences in study design our prevalence was the exact same at 42% (269/872). The increased prevalence of PTSD in the veteran population should be taken into consideration in interpreting these results.[15] Sexual trauma has been previously hypothesized as a risk factor for IC/BPS which is why we focused on this form of trauma specifically. A 2007 survey study by Peters et al. reported 37% of women with IC/BPS had a history of abuse compared to 22% of controls and 68% of women reporting abuse classified it as sexual. [16] A later questionnaire study by Nickel et al. found 24% of IC/BPS patients reported sexual trauma before age 17 compared to 15% of controls. [17] We observed a two-fold increase in sexual trauma in the female IC/BPS population but a complete lack of sexual trauma in the male IC/BPS population. Consideration should be given to the fact that sexual trauma is known to be underreported, particularly in males, and according to some reports is disclosed to medical personal less than 10% of the time.[18] Underreporting of sexual trauma could skew our results and makes it difficult to comment on the strength of this association. Overall, our results bolster the existing literature that these psychosocial comorbidities are more common among IC/BPS patients and vary by sex. Ellucidating these psychosocial comorbidities is of particular importance because of the recipricol relationship between psychological distress and chronic pain. There is potential for these conditions to significantly worsen IC/BPS symtpoms and therefore negatively impact the quality of life for IC/BPS patients.[7] Further awareness of this association may encourage clinicians to screen and seek intervention for IC/BPS patients who may suffer from these psychosocial comorbidities.

The association between IC/BPS and comorbidities linked with lifestyle and health behavior, such as smoking and alcohol abuse has remained conflicting. Several studies have suggested cigarette smoking increases risk for bladder pain symptoms, but a causal relationship has yet to be determined.[8, 19] Other studies' results have reflected our findings of a lack of association between smoking and IC/BPS.[20,21] Similarly, the literature regarding diabetes is controversial. Some studies demonstrate an association with IC/BPS symptoms; however, our findings do not support a greater prevalence in IC/BPS patients compared to non-IC/BPS patients. [8, 21] One of the few studies investigating alcohol abuse and IC/BPS was conducted in Taiwan and demonstrated IC/BPS patients had a significantly higher prevalence of alcohol abuse than controls (0.5% *vs.*0.2%).[22] While we did not find a relationship between alcohol abuse and IC/BPS, alcohol consumption is thought to exacerbate IC/BPS symptoms and is not recommended for IC/BPS patients.[23] Separate analysis performed to further adjust all modeling in this study for patient factors of diabetes, smoking, and alcohol abuse did not

influence any results given the lack of associations observed for these factors with IC (data not shown).

Our study design presents several limitations to take into consideration. First, we utilized a cohort of veterans who are known to have a higher prevalence of comorbidities, such as PTSD, depression, and substance use disorder than the general public.[15, 24] We also relied on ICD-9/ICD-IO codes to indicate whether patients had a diagnosis of IC/BPS and any comorbidity diagnosis other than smoking history. Our results may be affected by the potential misdiagnosis of IC/BPS and under or overdiagnosis of some comorbidities. Additionally, utilizing a pre-existing dataset limited our ability to select ICD-9/ICD-10 codes most suited to our investigation. Consequently, N30.11 was not included as an IC/BPS code and Major Depressive Disorder was the only depression code included in our "history of depression" category. Our IC/BPS cohort was older than the non-IC/BPS cohort, and while all analyses were adjusted for age, the presence of latent factors associated with age may have contributed to the increased comorbidities observed in this group. Our cohort included patients diagnosed with IC/BPS before and after the the transition to ICD-IO codes (October 1, 2015). However, this limitation is mitigated by our sensitivity analysis that did not reveal any significant difference in the prevalence of the comorbidities before and after October 1, 2015. Lastly, our study design required mining a large database, which presupposes all coding is accurate. There is potential for human error in this process and loss of granularity of the data.

CONCLUSION

In this nationwide, heterogenous population of veterans, patients with an IC/BPS diagnosis were more likely to have NUAS and psychosocial comorbidities than patients without IC/BPS. This validates previous studies that yielded similar results. The prevalence of comorbidities related to health behavior (smoking and alcohol abuse) and diabetes did not significantly differ between cohorts, suggesting they are not associated with IC/BPS diagnosis, though whether they affect IC/BPS symptoms could not be tested in our study. Future studies are needed to examine whether the comorbidities we evaluated are causally linked to IC/BPS. Doing so may shed light on risk factors for IC/BPS as well as conditions that are likely to arise after an IC/BPS diagnosis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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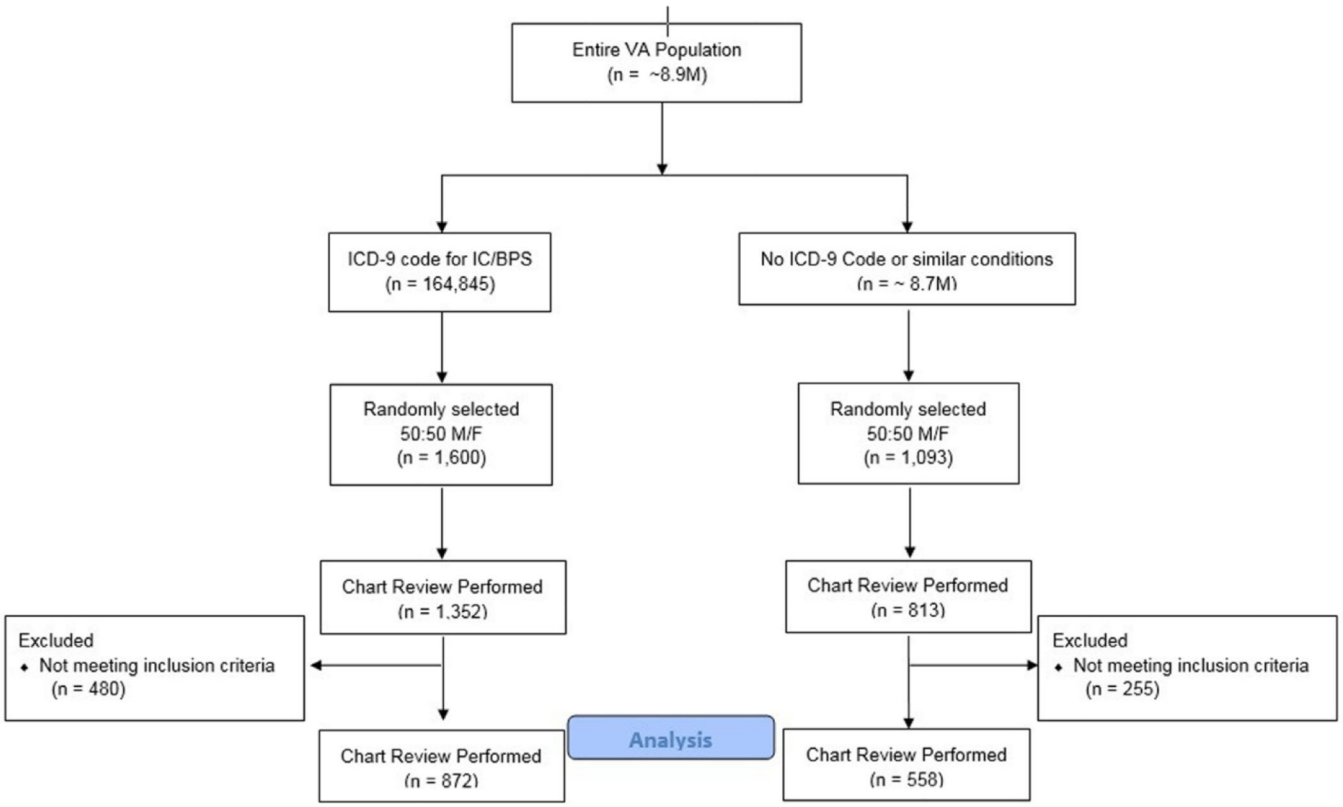

Fig. 1.
Study flow diagram.

Table 1.

Overall patient characteristics and comorbidities

	IC Patients (*n* = 872)		Non-IC Patients (*n* = 558)		OR (95% CI)	*P*-value
Age at Analysis	57.1+/−15.3		53.9 +/−16.2		-	< 0.001 *
Age at IC Diagnosis	49.4 +/−14.4		-			
Gender						
Male	355	41%	291	52%	-	< 0.001 †
Female	517	59%	267	48%		
Race/Ethnicity						
White	602	69%	332	60%	-	0.001 †
African American	181	21%	141	25%		
Hispanic	62	7%	48	9%		
Asian/Pac Islander	14	2%	16	3%		
Native American	7	1%	5	1%		
Unknown	6	1%	16	3%		
History of Tobacco Use	431	49%	306	55%	.81 (.64,1.0)	0.067 §
#Comorbidities	2.72+/−1–77		1.73 +/−1.30		-	< 0.001 ‡
Any Comorbidity	801	92%	468	84%	2.2 (1.5, 3.1)	< 0.001 §
Back Pain	668	77%	336	60%	2.2 (1.7, 2.8)	< 0.001 §
Diabetes	195	22%	117	21%	1.1 (.81,1.4)	0.626 §
NUAS ‖	388	45%	101	18%	3.5 (2.7, 4.6)	< 0.001 §
Chronic Fatigue Syndrome	49	6%	8	1%	3.6 (1.7, 7.7)	0.001 §
Fibromyalgia	258	30%	51	9%	3.7 (2.6, 5.1)	< 0.001 §
IBS	200	23%	37	7%	4.1 (2.8, 6.0)	< 0.001 §
Migraines	69	8%	23	4%	1.9 (1.1, 3.1)	0.014 §
Psychosocial ¶	529	61%	256	46%	1.9 (1.5, 2.4)	< 0.001 §
Alcohol Abuse	105	12%	55	10%	1.4 (.96, 2.0)	0.083 §

	IC Patients (n = 872)		Non-IC Patients (n = 558)		OR (95% CI)	P-value
PTSD	269	42%	161	29%	2.0 (1.5, 2.5)	< 0.001[§]
Sexual Trauma	65	8%	18	2%	2.1 (1.2, 3.6)	0.010[§]
Depression History	398	46%	161	29%	2.0 (1.6, 2.6)	< 0.001[§]

Data tested across groups with:

[*] Student's t-test

[†] Chi-square test

[‡] age, sex, and race adjusted Poisson regression, or

[§] age, sex, and race adjusted logistic regression.

[‖] NUAS includes chronic fatigue syndrome, fibromyalgia, IBS, & migraine.

[¶] Psychosocial includes alcohol abuse, PTSD, sexual trauma, depression history.

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Table 2.

Patient Comorbidities across Gender

	Female						Male						F vs. M IC Patients	
	IC Patients (*n* = 517)		Non-IC Patients (*n* = 267)		OR (95% CI)	*P*-value	IC Patients (*n* = 355)		Non-IC Patients (*n* = 291)		OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age at Analysis	50.5 +/−12.3		47.1+/−13.9		-	0.007*	66.7+/−14.2		60.1+/−15.8		-	<0.001*	-	<0.001*
Age at IC Diagnosis	43.1 +/−11.7		-		-	-	58.6 +/−14.2		-		-	-	-	<0.001*
History of Tobacco Use	223	43%	119	45%	.89 (.59,1.3)	0.877≠	208	59%	187	64%	.71 (.46,1.1)	0.216≠	.59 (.40, .90)	0.007≠
#Comorbidities	3.19+/−1–78		2.00+/−1.40			< 0.001†	2.05 +/−1–54		1.49 +/−1.15			<0.001†		< 0.001†
Any Comorbidity	495	96%	234	88%	3.4 (1.6, 7.2)	< 0.001≠	306	86%	234	80%	1.7 (.96, 3.0)	0.083≠	2.6 (1.2, 5.4)	0.005≠
Back Pain	427	83%	173	65%	2.8 (1.7, 4.3)	< 0.001≠	241	68%	163	56%	1.8 (1.2, 2.8)	0.003≠	1.8 (1.2, 2.9)	0.004≠
Diabetes	84	16%	33	12%	1.3 (.74, 2.4)	0.618≠	111	31%	84	29%	.93 (.59,1.5)	0.982≠	.65 (.40,1.1)	0.098≠
NUAS§	296	57%	69	26%	3.8 (2.5, 5.9)	< 0.001≠	92	26%	32	11%	3.0 (1.4, 5.0)	<0.001≠	3.5 (2.3, 5.4)	<0.001≠
Chronic Fatigue Syndrome	37	7%	5	2%	3.7(1.1,13.0)	0.033≠	12	3%	3	1%	3.3(6.1,17.5)	0.272≠	2.3 (.86, 6.1)	0.131≠
Fibromyalgia	214	41%	35	13%	4.4 (2.6, 7.5)	< 0.001≠	44	12%	16	6%	2.2 (1.0, 4.9)	0.041≠	6.1(3.6,10.5)	<0.001≠
IBS	154	30%	26	11%	3.6 (2.0, 6.4)	< 0.001≠	46	13%	8	3%	5.7(2.1,15.9)	<0.001≠	2.5 (1.4, 4.2)	<0.001≠
Migraines	58	11%	17	6%	1.9 (.91, 4.1)	0.115≠	11	3%	6	2%	1.7 (.46, 6.6)	0.716≠	3.0, (1.2, 7.5)	0.015≠
Psychosocial‖	366	71%	151	57%	2.0 (1.3, 3.1)	< 0.001≠	163	46%	105	36%	1.8 (1.2, 2.9)	0.002≠	1.9 (1.3, 2.8)	<0.001≠
Alcohol Abuse	61	12%	20	8%	1.7 (.85, 3.4)	0.202≠	44	12%	35	12%	.69 (.60, 2.1)	0.956≠	.76 (.42,1.4)	0.645≠
PTSD	261	51%	99	37%	2.0 (1.3, 2.9)	< 0.001≠	108	30%	62	21%	1.4 (1.2, 3.3)	0.002≠	1.6 (1.1, 2.4)	0.021≠
Sexual Trauma	65	13%	16	6%	2.3 (1.1, 5.0)	0.022≠	0	0%	2	1%	non-est	non-est	non-est	non-est
Depression History	287	56%	107	40%	1.9 (1.4, 3.3)	< 0.001≠	111	31%	54	19%	2.2 (1.3, 3.7)	< 0.001c	2.2 (1.4, 3.3)	<0.001≠

Data tested across groups with gender and age-adjusted

*linear regression

† age, sex, and race adjusted Poisson regression, or

‡ age, sex, and race adjusted logistic regression.

§ NUAS includes chronic fatigue syndrome, fibromyalgia, IBS, & migraine.

‖ Psychosocial includes alcohol abuse, PTSD, sexual trauma, depression history.