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A Review of the Evidence for Overlap between Urological and Non-urological Unexplained Clinical Conditions

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Abstract

Purpose—Unexplained clinical conditions share common features, such as pain, fatigue, disability out of proportion to physical examination findings, inconsistent laboratory abnormalities, and an association with stress and psychosocial factors. In this literature review, we examine the extent of the overlap among urological and non-urological unexplained clinical conditions characterized by pain, note the limitations of previous research, and suggest several possible explanatory models.

Materials & Methods—Using hallmark symptoms and syndromes as search terms, a search of 12 databases identified 1,037 full-length published articles in 8 languages from 1966 to April, 2008. The search focused on the overlap of chronic pelvic pain, interstitial cystitis, painful bladder syndrome, chronic prostatitis/chronic pelvic pain syndrome, or vulvodynia, with fibromyalgia, chronic fatigue syndrome, temporomandibular disorder, or irritable bowel syndrome. Information on authorship, type of case and control groups, eligibility criteria, case definitions, study methods, and major findings were abstracted.

Results—The literature suggests considerable comorbidity between urological and non-urological unexplained clinical conditions. The most robust evidence for overlap was for irritable bowel syndrome and urological unexplained syndromes, with some estimates of up to 79% comorbidity between chronic pelvic pain and symptoms of irritable bowel syndrome. However, most studies were limited by methodological problems, such as varying case definitions and selection of control subjects.

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Dr. Buchwald has full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Ms. Bullones Rodríguez made substantial contributions to the conception and design, acquisition of data, analysis and interpretation, drafting of the manuscript, and technical support. Dr. Afari made substantial contributions to conception and design, acquisition of data, analysis and interpretation, drafting of the manuscript, critical revision of the manuscript for important intellectual content, and obtaining funding. Dr. Buchwald made substantial contributions to conception and design, critical revision of the manuscript, obtaining funding, and supervision.

Conclusions—Overlap between urological and selected non-urological unexplained clinical conditions is substantial. Future research should focus on using standardized definitions and rigorously designed and well-controlled studies to further assess comorbidity, clarify the magnitude of the association, and examine common pathophysiological mechanisms.

Keywords

Chronic Fatigue Syndrome; Chronic Prostatitis; Fibromyalgia; Interstitial Cystitis; Temporomandibular Disorder

INTRODUCTION

Functional somatic syndromes, medically unexplained symptoms, somatoform disorders, and unexplained clinical conditions are common names given to conditions characterized by a lack of clear physical or biological etiology or an inconsistent demonstration of laboratory abnormalities.¹ These conditions are further characterized by symptoms such as pain, fatigue, sleep disturbances, and disability. The literature suggests that many of these conditions also share demographic characteristics, clinical course, and psychosocial profiles.¹ The diagnosis given to a patient suffering from one of these conditions often depends on the hallmark symptom and the expertise of the treating clinician rather than on the illness itself.¹ The frequency of co-diagnosis and the common features shared by unexplained clinical conditions have become topics of growing interest over the past few years.

Physicians have been challenged to diagnose and appropriately treat patients with such unexplained clinical conditions as fibromyalgia (FM), chronic fatigue syndrome (CFS), temporomandibular disorder (TMD), irritable bowel syndrome (IBS), chronic pelvic pain (CPP), interstitial cystitis (IC), painful bladder syndrome (PBS), chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS), and vulvodynia. A recent review found that patients with IC often suffered from other unexplained conditions and symptoms.² Although a substantial body of literature has examined the comorbidity of non-urological unexplained clinical conditions such as FM, CFS, and IBS,³ the extent of the overlap between urological and non-urological unexplained clinical conditions, and the potential mechanisms for their co-occurrence, remain largely unknown.

The recent emphasis by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) on a multidisciplinary approach to the study of urological chronic pelvic pain syndromes, further underscores the need to examine and understand the overlap between urological and non-urological unexplained clinical conditions (<http://www2.niddk.nih.gov/Research/ScientificAreas/Urology/MAPP>). We have, therefore, conducted an exhaustive review of the literature on comorbidity between the most common urological pelvic pain syndromes (i.e., CPP, IC, PBS, CP/CPPS, and vulvodynia) and the non-urological conditions of FM, CFS, TMD, and IBS. Our review focused on overlap with these non-urological conditions for several reasons. First, our goal was to examine overlap among conditions with a significant pain component which ruled out overlap with psychiatric conditions such as panic disorder that also have been shown to co-occur with urological pelvic pain syndromes. Second, frequently comorbid pain conditions with known physical or biological etiology were not included since they would not satisfy the definition of unexplained clinical conditions. Third, these 4 non-urological conditions were the focus of most data-based articles in the existing literature and were of particular interest to NIDDK. Finally, these non-urological conditions differed in the location of pain, which could influence the extent of overlap between urological and non-urological unexplained clinical conditions.

MATERIALS AND METHODS

Search Strategy

Articles were identified by a search of the following databases: PubMed (1966-April 2008), CINAHL (1981-April 2008), CochraneCollaboration Reviews (1993-April 2008), Current Contents (2000-April 2008), EBCO Academic Search Premier (1975-April 2008), EMBASE (1974-April 2008), ISI Web of Science (1980-April 2008), PsychInfo(1967-April 2008), Science Citation Indexes (1996-April 2008), and Scirus, Scopus, and Google Scholar (April 2008).

Our initial search included the following search terms for the 5 urological unexplained clinical conditions: *chronic pelvic pain*, *interstitial cystitis*, *painful bladder syndrome*, *chronic prostatitis*, and *vulvodynia*, in combination with 4 non-urological unexplained clinical conditions: *chronic fatigue syndrome*, *fibromyalgia*, *temporomandibular disorder*, and *irritable bowel syndrome*. The Medical Subject Headings were combined with truncated keywords that described the symptoms of the various conditions. All possible combinations of the 2 sets of search terms were examined.

Next, we looked for all search terms individually and in combination with the words *overlapping*, *overlap*, *comorbidity*, and *comorbid*. In addition, we combined the terms for the hallmark symptoms associated with each non-urological condition with the hallmark symptoms associated with each urological condition (e.g., *chronic fatigue* and *painful bladder*). Bibliographies of relevant articles were examined to identify any other reports that may have been missed. Finally, members of the NIDDK's Working Group on Urological Chronic Pelvic Pain, a group of experts in the fields of urology, rheumatology, epidemiology, and internal medicine (see Acknowledgments section for full list of Working Group members), were contacted to review the list of relevant articles and to locate other pertinent peer-reviewed publications. Together, these search strategies yielded 1,037 unique publications.

Inclusion Criteria

Articles included in this review examined the comorbidity or overlap of at least 1 urological condition or hallmark symptom with at least 1 non-urological condition or hallmark symptom. We focused on articles in English, Hebrew, German, French, Spanish, Korean, Japanese, and Russian, because they could be reviewed by the authors or members of the Working Group. No limits were placed on participant age, but all relevant articles pertained to adults, most of whom were women.

We reviewed 2 types of studies: comparison and single-condition. The first type compared two or more groups diagnosed with different unexplained clinical conditions (e.g., IC versus FM patients) to each other, or compared one group diagnosed with an urological unexplained clinical condition to a healthy control group (e.g., CP patients versus healthy volunteers). The single-condition studies examined participants with a specific unexplained clinical condition or symptom for the co-occurrence of other conditions (e.g., frequency of vulvar pain in IBS or frequency of IBS in vulvodynia). Comparison studies can more precisely estimate the extent of comorbidity or overlap than can single-condition studies, and they can highlight potential similarities in pathophysiology across conditions.

Studies that were initially excluded because they did not meet the overlap criterion were reviewed again for possible incidental findings on the overlap of urological and non-urological conditions that may have been reported as part of the data analysis or in the context of other study findings. The initially-excluded studies that were deemed relevant upon further review are included in the tables, as indicated.

Exclusion Criteria

Most (90%) of articles that we identified were excluded because they did not examine the overlap between urological and non-urological conditions. Other articles were excluded for the following reasons: the main patient group did not have an unexplained clinical condition (e.g., migraine or panic); the article focused on an unexplained clinical condition or symptom not considered here, or presented data on broad symptom categories that included conditions other than the ones considered here (e.g., functional digestive disorders); despite mentioning overlap, the article lacked relevant data; or the main topic was not pertinent to our review (e.g., abuse or pharmacological treatment approaches). Articles that did not present primary data, such as reviews, were not included in our analysis or tables even if they supported our findings and conclusions.

Data Extraction and Synthesis

Based on the aforementioned inclusion and exclusion criteria, 41 relevant publications were identified and are reported here.¹ For each study, we extracted information on study characteristics (e.g., name of first author and publication year), type of participant group (e.g., patients or community participants), group sample sizes, diagnostic criteria, methods, and major findings. The initial review findings were examined by a second reviewer who independently extracted the above information from the relevant publications. Members of the Working Group reviewed drafts of the findings for completeness of the literature review and contributed to the synthesis and interpretation of the findings. The final findings of the review were endorsed by, and represent the views of, the authors and the Working Group.

RESULTS

Overlap of Symptoms and Syndromes in Comparison Studies

We found 25 publications on comparison studies that provided data on the comorbidity of urological and non-urological unexplained clinical conditions or symptoms (Table 1). Although some of the studies were published in the early 1990s, most (68%) were published since 2005. Of these 25 studies, 19 reported on patient populations and 6 reported on non-clinical samples derived from population surveys. The studies used diverse diagnostic approaches, including physician diagnoses, symptom-based definitions, and more rigorous, well-established criteria such as the NIDDK criteria for IC diagnosis or the American College of Rheumatology criteria for fibromyalgia. Study methods included self-report questionnaires on medical history, standardized surveys and interviews, physician and tender point examinations, and computerized reviews of International Classification of Diseases-9 codes.

Sixteen studies reported data on the overlap between urological unexplained clinical conditions and musculoskeletal conditions or symptoms such as FM or chronic widespread pain, joint pain, generalized pain, or myalgia.^{4–19} However, only 4 studies were specifically designed to examine the comorbidity of FM or chronic widespread pain with one of the urological conditions.^{5,8,14,15} About 9% to 12% of IC patients also experienced FM,^{5,14} and 23% to 27% of FM patients had symptoms consistent with IC.⁵ One of the earliest studies found that 68% of men and 66% of women with FM also reported pelvic pain symptoms.⁴ A twin study that controlled for genetic and environmental confounding found that approximately 23% of twins with chronic widespread pain and 11% of their pain-free co-twins reported urinary tract problems.⁹ Although the overlap between CP/CPPS and FM has not been directly examined, one study observed that 21% of individuals with CP/CPPS symptoms reported a history of musculoskeletal, rheumatological, or connective tissue diseases,¹¹ and another noted a trend

¹A complete list of references for these publications is available from authors by request.

for higher manual tender point examination scores in CP/CPPS patients than in controls.¹⁶ Vulvodynia has also been described as co-occurring with FM.^{8,15}

Only 3 studies, all of them on non-clinical populations, examined the overlap between urological unexplained clinical conditions and CFS. One study of twin pairs discordant for various definitions of chronic fatigue or CFS found that fatigued twins were up to 20 times more likely to have IC, and up to 6 times more likely to have chronic pelvic pain, than their non-fatigued co-twins.²⁰ Conversely, CFS was reported more than twice as often by individuals with CP/CPPS symptoms than by asymptomatic age-matched controls.¹¹ Likewise, individuals with vulvodynia more often reported CFS than did asymptomatic controls.¹⁵ We did not find comparative studies on overlap between TMD and any urological unexplained clinical condition.

Finally, more than half of the comparison studies (15 of 25) examined the overlap among urological unexplained clinical conditions and IBS. Several studies, using different methods, reported that 7% to 48% of patients with IC or symptoms of PBS also had IBS.^{10,14,21,22} Others found that patients with IC were 11 times more likely to be diagnosed with IBS than were control participants.²³ Further, 22% of men with CP/CPPS or its symptoms had IBS.^{11,19,22} Likewise, 37% of women with chronic pelvic pain met the criteria for IBS.²⁴ Conversely, one study found that 35% of IBS patients, but only 14% of patients with inflammatory bowel disease, reported symptoms of chronic pelvic pain.²⁵ In other studies, IBS was associated with increased probability of an IC diagnosis and increased urinary symptom scores.^{13,26,27} Vulvodynia has also been documented as comorbid with IBS.^{8,15,28}

Overlap of Symptoms and Syndromes in Single-Condition Studies

We found 16 publications that assessed individuals with a single unexplained clinical condition for the presence of at least 1 additional syndrome or hallmark symptom (Table 2). Despite methodological differences, the results of these investigations are generally consistent with those in Table 1. A study of patients with chronic pelvic pain symptoms found that 19% also had FM symptoms and 8% had CFS symptoms.²⁹ These rates are similar to those noted in other publications of self-reported FM (17%) and CFS (9%) in individuals with IC³⁰ and vulvar pain.³¹ Conversely, a recent study that used the American College of Rheumatology criteria for FM found that 11% of IC patients met the diagnostic criteria for FM.³² Additionally, 2 studies provided data on the overlap between TMD and at least 1 urological unexplained clinical condition. One study found that 13% of patients with TMD had a history of IC,³³ and the other reported that almost 20% of women with vulvar pain reported TMD.³¹

Most of the single-condition studies examined the comorbidity of urological unexplained clinical conditions and symptoms with IBS. These studies reported that 30% to 75% of individuals with IC or IC symptoms had IBS or IBS symptoms,^{30,34,35} and 26% to 56% of IBS patients reported urinary problems.^{36,37} Likewise, 19% to 79% of patients with chronic pelvic pain had IBS or IBS symptoms.^{29,38–40} Among women with vulvar pain, 35% reported IBS.³¹

DISCUSSION

Evidence of Overlap

Our extensive review of the literature on urological and non-urological unexplained clinical conditions found a small but growing body of published reports documenting the comorbidity of these conditions. The most robust evidence for overlap exists for IBS and unexplained urological conditions, in terms of both the number of publications and the relative consistency of results across studies. This overlap may reflect either a publication bias or the anatomical

fact that urological chronic pelvic pain conditions and IBS occur in a similar region of the body and involve visceral pain sensations. In contrast, the few studies on FM, CFS, and TMD suggest a more modest comorbidity with urological unexplained clinical conditions. Nonetheless, our findings generally support previous assertions of overlap among some or all of the urological and non-urological unexplained clinical conditions.^{2,3,41}

The common sociodemographic and clinical features shared by these conditions, the symptom overlap in many of the case definitions, and the tendency to respond to the same therapies, have led several investigators to suggest that all unexplained clinical conditions are different manifestations of the same underlying pathophysiological process.^{1,3} Additionally, some experts have argued that the comorbidity of FM, CFS, TMD, and IBS could result from similarities in their case definitions.¹ Although this explanation may apply to the overlap between urological pelvic pain conditions and IBS,⁴¹ urinary and pelvic pain symptoms are not part of the symptom criteria for FM, CFS or TMD. Thus, commonalities in symptom criteria cannot completely account for the overlap summarized in this review. Nonetheless, the heterogeneity of these conditions, especially sub-groups of patients with uncharacteristic symptoms, can account, in part, for the substantial overlap between these conditions.

Proposed Explanations

Despite decades of research on unexplained clinical conditions, their etiology and pathophysiology remain elusive. We identify 3 dominant perspectives on the mechanisms for these conditions: 1) physiological processes, particularly neuroendocrine, immunological, and neurotransmitter dysfunction in the central nervous system; 2) victimization, abuse, and trauma; and 3) psychological distress, psychiatric disorders, stress tolerance, and recovery from stress.³ Although abnormalities have been demonstrated across several domains that are consistent with all of these perspectives, most studies have examined only single hypotheses. In addition, many affected patients do not exhibit neuroendocrine abnormalities, do not suffer from depression or other psychiatric conditions, and have not been abused or victimized. Organ-based approaches (i.e., examining the bladder, prostate, or skeletal system) have similarly failed to provide useful insights into the etiologies of, or effective treatments for, these conditions. In general, research on urological chronic pelvic pain conditions and similar disorders has not been able to distinguish epiphenomena from underlying pathophysiology.

A multidimensional conceptual model seems better suited to guide research and understanding, both of the conditions themselves and of their co-occurrence.¹ A multidimensional model can encompass the range of predisposing (e.g., genetic and environmental influences, physiological perturbations), precipitating (e.g., trauma, infections), and perpetuating (e.g., central sensitization, perceptual amplification) factors, as well as predictors of chronicity (e.g., psychological and sleep disturbances) that are necessary but not individually sufficient for developing 1 or more unexplained clinical conditions (see Figure). A strength of this conceptualization is that it incorporates the 2 most prominent overarching theories of pain in order to facilitate the understanding and treatment of unexplained clinical conditions. The diathesis-stress model takes into account both the predisposing biological and genetic factors as well as the environmental and life events that interact to trigger behaviors and disorders.⁴² Alternately, the gate control theory of pain and its more recent expansion emphasize the role of the brain and its interaction with cognitive and emotional factors in pain transmission and modulation.⁴³ The multidimensional model presented here combines these overarching theories to offer multiple hypotheses that test similarities in vulnerability factors and stressors, as well as the central affective, sensory, cognitive, motor, inhibitory, and autonomic responses involved in pain processing. Elements of this model has spurred a small but growing body of literature, especially in pain sensitivity and its enhanced perception, and central sensitization of pain in FM and CFS,^{44,45} and support the presence of basic similarities across these

conditions. A more broadly based conceptual model can facilitate interdisciplinary linkages among the basic, clinical, and population sciences to investigate their etiology, clinical manifestations, comorbidity, and prognosis.

Conceptually driven investigations of the mechanisms that may predispose, precipitate, perpetuate, and predict these conditions can improve our understanding of urological unexplained clinical conditions and their comorbidities. Given the prominence of pain across the syndromes of interest, an examination of the central sensitization hypothesis is crucial to understanding their substantial comorbidity. Further, twin and family studies can clarify the role of shared genetic and environmental factors in their genesis and perpetuation.

Limitations of Studies

Our review discovered several methodological shortcomings in the literature that undermine the strength of our conclusions and limit comparability across studies. First and foremost, study participants were drawn primarily from tertiary care clinics, hampering the generalizability of findings both to primary care patients and to the general population. Clinical ascertainment and other biases associated with the study of treatment-seeking populations are well known,⁴⁶ and can be an important source of spurious comorbidity. Anxiety, poor coping, stressful events, and other psychological factors also may play a role in health-care seeking in IBS and FM.⁴⁷ Thus, the comorbidity of urological and non-urological unexplained clinical conditions may be an artifact of healthcare use.

Second, we found inconsistencies in assessment. Although research on unexplained clinical conditions may be hampered by a lack of diagnostic markers, all of these conditions have established case definitions that are designed to facilitate symptom-based diagnoses as well as comparability across research studies. Nonetheless, many different methods were used to assess the conditions of interest, ranging from the use of established case definitions to self-report of physician diagnoses and review of computerized ICD-9 codes. Several investigations relied on medical history questionnaires or self-reported diagnoses without independent confirmation by medical record reviews or clinical examinations. This reliance calls into question the accuracy of all rates of conditions based on self-report, but especially those that require physical examination findings (e.g., FM) or exclusion of specific medical disorders (e.g., CFS). In addition, studies based on physician diagnoses in medical records may underestimate comorbidity if a patient attends one clinic for primary symptoms but is discouraged from seeking specialty care for other symptoms, as may occur in health maintenance organizations. Studies also differed in inclusion and exclusion criteria. All of these factors affect the degree of overlap among urological and non-urological unexplained clinical conditions and make comparisons across studies problematic.

Third, with the exception of CP/CPPS in men, most participants with unexplained clinical conditions were women. It has been debated whether certain urological unexplained clinical conditions, particularly IC/PBS and CP/CPPS in men, represent somewhat different manifestations of the same disorder and whether the risk factors and manifestations of IC/PBS differ in men and women.⁴⁸ Sex differences clearly do exist in the epidemiology, symptomatology, physiology, and psychological features of FM, CFS, and IBS,⁴⁹ raising the possibility that the overlap between urological and non-urological unexplained clinical conditions is sex-specific. Clearly, there are too few studies in men to fully examine any sex differences in overlap that may exist. Studies with large samples of men are needed to examine the role of sex in the co-occurrence of these conditions. Likewise, more data are needed to examine the association of these conditions across different cultural, racial, and ethnic groups. Finally, in the studies that compared 2 or more groups, the control groups consisted variously of healthy individuals, those with other chronic illnesses, or controls whose health status was unreported. Only 2 investigations controlled for genetic and common environmental effects

by using co-twin control methods,^{9,20} and most studies did not use multivariate analytic techniques to adjust for demographic or other differences that could reduce the strength of the association between comorbid conditions.

CONCLUSIONS

Our extensive review of the published literature on the overlap between urological and non-urological unexplained clinical conditions suggests that comorbidity is frequent. However, these studies suffer from several methodological shortcomings that undermine the strength of our conclusions and limit comparability across studies. Future studies examining the overlap should adhere to the established research diagnostic criteria for each condition. Large scale, rigorously designed, and well-controlled studies in both clinical and community populations can yield more definitive answers to questions of overlapping symptoms and syndromes. Additionally, longitudinal cohort designs are needed to examine their risk factors, their temporal onset, and their prognosis. A recent study published since this review was undertaken found significant associations between antecedent non-urological unexplained clinical conditions and incident cases of IC/PBS,⁵⁰ further underscoring the need for longitudinal studies. Other studies of urological unexplained clinical conditions should focus on health- and behavior-related characteristics – for example, quality of life, disability, or health care use – that can estimate the added burden of co-occurring syndromes on meaningful outcomes such as functional status, employment, and health care costs. Examining possible mediators for comorbidity – for example, abuse, victimization, or psychological distress – can elucidate the relationship between overlapping conditions and identify subgroups at risk for developing urological chronic pelvic pain syndromes and related conditions. Well-controlled studies to assess comorbidity and pathophysiological mechanisms can advance our understanding and improve the treatment of these conditions.

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References

1. Wessely S, Nimnuan C, Sharpe M. Functional somatic syndromes: one or many? *Lancet* 1999;354:936–9. [PubMed: 10489969]
2. Buffington CA. Comorbidity of interstitial cystitis with other unexplained clinical conditions. *J Urol* 2004;172:1242–8. [PubMed: 15371816]
3. Aaron LA, Buchwald D. A review of the evidence for overlap among unexplained clinical conditions. *Ann Intern Med* 2001;134:868–81. [PubMed: 11346323]
4. Waylonis GW, Heck W. Fibromyalgia syndrome. New associations. *Am J Phys Med Rehabil* 1992;71:343–8. [PubMed: 1466872]
5. Clauw DJ, Schmidt M, Radulovic D, Singer A, Katz P, Bresette J. The relationship between fibromyalgia and interstitial cystitis. *J Psychiatr Res* 1997;31:125–31. [PubMed: 9201654]
6. Ostensen M, Schei B. Sociodemographic characteristics and gynecological disease in 40–42 year old women reporting musculoskeletal disease. *Scand J Rheumatol* 1997;26:426–34. [PubMed: 9433402]

7. Erickson DR, Morgan KC, Ordille S, Keay SK, Xie SX. Nonbladder related symptoms in patients with interstitial cystitis. *J Urol* 2001;166:557–61. discussion 561–2. [PubMed: 11458068]
8. Arnold LD, Bachmann GA, Rosen R, Kelly S, Rhoads GG. Vulvodynia: characteristics and associations with comorbidities and quality of life. *Obstet Gynecol* 2006;107:617–24. [PubMed: 16507933]
9. Kato K, Sullivan PF, Evengard B, Pedersen NL. Chronic widespread pain and its comorbidities: a population-based study. *Arch Intern Med* 2006;166:1649–54. [PubMed: 16908799]
10. Kennedy CM, Bradley CS, Galask RP, Nygaard IE. Risk factors for painful bladder syndrome in women seeking gynecologic care. *Int Urogynecol J Pelvic Floor Dysfunct* 2006;17:73–8. [PubMed: 15995790]
11. Pontari MA. Chronic prostatitis/chronic pelvic pain syndrome and interstitial cystitis: are they related? *Curr Urol Rep* 2006;7:329–34. [PubMed: 16930505]
12. Shaver JL, Wilbur J, Robinson FP, Wang E, Buntin MS. Women's health issues with fibromyalgia syndrome. *J Womens Health (Larchmt)* 2006;15:1035–45. [PubMed: 17125422]
13. Wu EQ, Birnbaum H, Kang YJ, Parece A, Mallett D, Taitel H, Evans RJ. A retrospective claims database analysis to assess patterns of interstitial cystitis diagnosis. *Curr Med Res Opin* 2006;22:495–500. [PubMed: 16574033]
14. Wu EQ, Birnbaum H, Mareva M, Parece A, Huang Z, Mallett D, Taitel H. Interstitial Cystitis: Cost, treatment and co-morbidities in an employed population. *Pharmacoeconomics* 2006;24:55–65. [PubMed: 16445303]
15. Arnold LD, Bachmann GA, Rosen R, Rhoads GG. Assessment of vulvodynia symptoms in a sample of US women: a prevalence survey with a nested case control study. *Am J Obstet Gynecol* 2007;196:128, e1–6. [PubMed: 17306651]
16. Berger RE, Ciol MA, Rothman I, Turner JA. Pelvic tenderness is not limited to the prostate in chronic prostatitis/chronic pelvic pain syndrome (CPPS) type IIIA and IIIB: comparison of men with and without CP/CPPS. *BMC Urol* 2007;7:17. [PubMed: 17908331]
17. Araujo MP, Faria AC, Takano CC, de Oliveira E, Sartori MG, Pollak DF, Girao MJ. Urodynamic study and quality of life in patients with fibromyalgia and lower urinary tract symptoms. *Int Urogynecol J Pelvic Floor Dysfunct*. 2008
18. Clemens JQ, Meenan RT, O'Keeffe Rosetti MC, Kimes TA, Calhoun EA. Case-control study of medical comorbidities in women with interstitial cystitis. *J Urol* 2008;179:2222–5. [PubMed: 18423759]
19. Dimitrakov J, Joffe HV, Soldin SJ, Bolus R, Buffington CA, Nickel JC. Adrenocortical hormone abnormalities in men with chronic prostatitis/chronic pelvic pain syndrome. *Urology* 2008;71:261–6. [PubMed: 18308097]
20. Aaron LA, Herrell R, Ashton S, Belcourt M, Schmaling K, Goldberg J, Buchwald D. Comorbid clinical conditions in chronic fatigue: a co-twin control study. *J Gen Intern Med* 2001;16:24–31. [PubMed: 11251747]
21. Koziol JA. Epidemiology of interstitial cystitis. *Urol Clin North Am* 1994;21:7–20. [PubMed: 8284848]
22. Clemens JQ, Brown SO, Kozloff L, Calhoun EA. Predictors of symptom severity in patients with chronic prostatitis and interstitial cystitis. *J Urol* 2006;175:963–6. discussion 967. [PubMed: 16469592]
23. Novi JM, Jeronis S, Srinivas S, Srinivasan R, Morgan MA, Arya LA. Risk of irritable bowel syndrome and depression in women with interstitial cystitis: a case-control study. *J Urol* 2005;174:937–40. [PubMed: 16093997]
24. Grace V, Zondervan K. Chronic pelvic pain in women in New Zealand: comparative well-being, comorbidity, and impact on work and other activities. *Health Care Women Int* 2006;27:585–99. [PubMed: 16844672]
25. Walker EA, Gelfand AN, Gelfand MD, Green C, Katon WJ. Chronic pelvic pain and gynecological symptoms in women with irritable bowel syndrome. *J Psychosom Obstet Gynaecol* 1996;17:39–46. [PubMed: 8860885]

26. Zimmerman J. Extraintestinal symptoms in irritable bowel syndrome and inflammatory bowel diseases: nature, severity, and relationship to gastrointestinal symptoms. *Dig Dis Sci* 2003;48:743–9. [PubMed: 12741465]
27. Whitehead WE, Palsson OS, Levy RR, Feld AD, Turner M, Von Korff M. Comorbidity in irritable bowel syndrome. *Am J Gastroenterol* 2007;102:2767–76. [PubMed: 17900326]
28. Kennedy CM, Nygaard IE, Bradley CS, Galask RP. Bladder and bowel symptoms among women with vulvar disease: are they universal? *J Reprod Med* 2007;52:1073–8. [PubMed: 18210896]
29. Nimnuan C, Rabe-Hesketh S, Wessely S, Hotopf M. How many functional somatic syndromes? *J Psychosom Res* 2001;51:549–57. [PubMed: 11595242]
30. Alagiri M, Chottiner S, Ratner V, Slade D, Hanno PM. Interstitial cystitis: unexplained associations with other chronic disease and pain syndromes. *Urology* 1997;49:52–7. [PubMed: 9146002]
31. Gordon AS, Panahian-Jand M, McComb F, Melegari C, Sharp S. Characteristics of women with vulvar pain disorders: responses to a Web-based survey. *J Sex Marital Ther* 2003;29 (Suppl 1):45–58. [PubMed: 12735088]
32. Yamada T, Funahashi M, Murayama T. Clinical evaluation of 30 patients with interstitial cystitis complicated by fibromyalgia. *Nippon Hinyokika Gakkai Zasshi* 2005;96:554–9. [PubMed: 16083033]
33. Korszun A, Papadopoulos E, Demitrack M, Engleberg C, Crofford L. The relationship between temporomandibular disorders and stress-associated syndromes. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1998;86:416–20. [PubMed: 9798224]
34. Giamberardino, M. Fillingim, R. Sex, gender and pain. Vol. 17. Seattle: IASP Press; 2000. Sex-related and hormonal modulation of visceral pain; p. 135–162.
35. FitzGerald MP, Brensinger C, Brubaker L, Probert K. What is the pain of interstitial cystitis like? *Int Urogynecol J Pelvic Floor Dysfunct* 2006;17:69–72. [PubMed: 15995791]
36. Maxton DG, Morris JA, Whorwell PJ. Ranking of symptoms by patients with the irritable bowel syndrome. *BMJ* 1989;299:1138. [PubMed: 2513023]
37. Blanchard EB, Keefer L, Lackner JM, Galovski TE, Krasner S, Sykes MA. The role of childhood abuse in Axis I and Axis II psychiatric disorders and medical disorders of unknown origin among irritable bowel syndrome patients. *J Psychosom Res* 2004;56:431–6. [PubMed: 15094028]
38. Walker EA, Katon WJ, Jemelka R, Alfrey H, Bowers M, Stenchever M. The prevalence of chronic pelvic pain and irritable bowel syndrome in 2 university clinics. *J Psychosom Obstet Gynaecol* 1991;12:65–75.
39. Williams RE, Hartmann KE, Sandler RS, Miller WC, Savitz LA, Steege JF. Recognition and treatment of irritable bowel syndrome among women with chronic pelvic pain. *Am J Obstet Gynecol* 2005;192:761–7. [PubMed: 15746669]
40. Fenton BW, Durner C, Fanning J. Frequency and Distribution of Multiple Diagnoses in Chronic Pelvic Pain Related to Previous Abuse or Drug-Seeking Behavior. *Gynecol Obstet Invest* 2008;65:247–251. [PubMed: 18196907]
41. Riedl A, Schmidtmann M, Stengel A, Goebel M, Wissner AS, Klapp BF, Monnikes H. Somatic comorbidities of irritable bowel syndrome: a systematic analysis. *J Psychosom Res* 2008;64:573–82. [PubMed: 18501257]
42. Turk DC. A diathesis-stress model of chronic pain and disability following traumatic injury. *Pain Res Manag* 2002;7:9–19. [PubMed: 16231063]
43. Melzack R. From the gate to the neuromatrix. *Pain Suppl* 1999;6:S121–6.
44. Gracely RH, Petzke F, Wolf JM, Clauw DJ. Functional magnetic resonance imaging evidence of augmented pain processing in fibromyalgia. *Arthritis Rheum* 2002;46:1333–43. [PubMed: 12115241]
45. Ullrich PM, Afari N, Jacobsen C, Goldberg J, Buchwald D. Cold pressor pain sensitivity in monozygotic twins discordant for chronic fatigue syndrome. *Pain Med* 2007;8:216–22. [PubMed: 17371408]
46. Bogenschutz MP, Nurnberg HG. Theoretical and methodological issues in psychiatric comorbidity. *Harv Rev Psychiatry* 2000;8:18–24. [PubMed: 10824294]
47. Ringstrom G, Abrahamsson H, Strid H, Simren M. Why do subjects with irritable bowel syndrome seek health care for their symptoms? *Scand J Gastroenterol* 2007;42:1194–203. [PubMed: 17852851]

48. Moldwin RM. Similarities between interstitial cystitis and male chronic pelvic pain syndrome. *Curr Urol Rep* 2002;3:313–8. [PubMed: 12149163]
49. Munce SE, Stewart DE. Gender differences in depression and chronic pain conditions in a national epidemiologic survey. *Psychosomatics* 2007;48:394–9. [PubMed: 17878497]
50. Warren JW, Howard FM, Cross RK, Good JL, Weissman MM, Wesselman U, Langenberg P, Greenberg P, Clauw DJ. Antecedent nonbladder syndromes in case-control study of interstitial cystitis/painful bladder syndrome. *Urology* 2009;73:52–7. [PubMed: 18995888]

Figure.
A multidimensional conceptual model of unexplained clinical conditions

Table 1

Overlap of symptoms and syndromes among urological and non-urological unexplained clinical conditions in studies comparing at least two groups, presented by year of publication.

First Author *	Year	Groups	Sample Size	Diagnostic Criteria	Study Methods	Major Findings
Waylonis	1992	<ul style="list-style-type: none"> FM patients Controls 	554 169	Physician diagnosis	Medical history questionnaire	<ul style="list-style-type: none"> 68.4% of the FM males vs. 0% of control males had pelvic pain 65.8% of the FM females vs. 33.3% of control females had pelvic pain
Kozioł	1994	<ul style="list-style-type: none"> IC patients Healthy controls Non-IC patients 	565 171	Physician diagnosis	Medical history questionnaire	<ul style="list-style-type: none"> 22.5% of IC patients vs. 6.7% of controls reported IBS ($p < 0.0001$)
Walker	1996	<ul style="list-style-type: none"> IBS patients IBD patients 	60 26	Physician diagnosis; symptom-based	Structured psychiatric interview; structured interview; medical and psychiatric history questionnaire	<ul style="list-style-type: none"> 35% of IBS patients vs. 13.8% of patients with IBD reported CPP ($p < 0.05$)
Clauw	1997	<ul style="list-style-type: none"> FM patients IC patients Controls 	60 30 30	ACR NIH IC criteria	Questionnaire assessing current and lifetime history of symptoms and syndromes; tender point examination	<ul style="list-style-type: none"> 12% of IC patients met FM criteria 23% of FM patients vs. 2% of controls had bladder fullness symptoms 23% of FM patients vs. 4% of controls had urinary urgency symptoms 27% of FM patients vs. 2% of controls had pelvic pain
Ostensen	1997	<ul style="list-style-type: none"> Individuals with musculoskeletal disorders Controls 	1,988 2,046	Symptom-based	Questionnaire assessing health problems; self-reported history of health problems and behaviors; health screening	<ul style="list-style-type: none"> 4% of women consulting for FM symptoms had gynecological symptoms including CPP
Aaron	2001	<ul style="list-style-type: none"> Twins with chronic fatigue or CFS Control twins 	127 127	Symptom-based	Questionnaires collecting data on demographics, habits, lifestyle, physical conditions, checklist of medical disorders; fatigue was classified	<ul style="list-style-type: none"> Fatigued twins at the 3 levels were 2–20 times more likely to have IC than their nonfatigued co-twins

First Author*	Year	Groups	Sample Size	Diagnostic Criteria	Study Methods	Major Findings
					according to 3 levels of stringency	<ul style="list-style-type: none"> Fatigued twins at the 3 levels were 3.5–6 times more likely to have CPP than their nonfatigued co-twins
Erickson	2001	<ul style="list-style-type: none"> IC patients Controls 	35 35	Physician diagnosis; NIDDK criteria	University of Wisconsin questionnaire	<ul style="list-style-type: none"> Patients with IC had higher scores than controls for other pelvic discomfort, backache, dizziness, chest pain, aches in joints, abdominal cramps, and headache ($p < 0.01$)
Zimmerman	2003	<ul style="list-style-type: none"> IBS patients IBD patients Controls 	53 55 56	Clinical criteria; Rome I criteria for IBS	Standardized questionnaire	<ul style="list-style-type: none"> IBS patients had higher urinary symptom scores than IBD patients ($p < 0.02$) and controls ($p < 0.001$)
Noxi	2005	<ul style="list-style-type: none"> IC patients Controls 	46 46	ICD-9	Standardized IC symptom questionnaire; Rome II standardized questionnaire for IBS	<ul style="list-style-type: none"> Women with IC were 11 times more likely to be diagnosed with IBS than controls (95% CI: 2.7–52, $p < 0.001$)
Arnold	2006	<ul style="list-style-type: none"> Vulvodynia patients Controls 	208 77	Physician diagnosis	Questionnaire assessing health history, use of health system, quality of life and vulvodynia	<ul style="list-style-type: none"> Patients with vulvodynia were 3.84 times more likely to report FM (95% CI: 1.54–9.55) and 3.11 times more likely to report IBS (95% CI: 1.60–6.05) than Controls
Clemens	2006	<ul style="list-style-type: none"> CP/CPPS patients IC patients (men were excluded) 	174 111	ICD-9	Questionnaires assessing medical history, life style, and reproductive history in females	<ul style="list-style-type: none"> 22.4% of CP/CPPS patients reported IBS 40% of IC patients reported IBS
Grace	2006	<ul style="list-style-type: none"> Individuals with CPPS Individuals with dysmenorrhea Individuals with dyspareunia Healthy controls 	286 286 110 397	Symptom-based; Rome II criteria	Postal questionnaire on issues related to women's health and functioning	<ul style="list-style-type: none"> 37.3% of women with CPP symptoms met IBS criteria

First Author*	Year	Groups	Sample Size	Diagnostic Criteria	Study Methods	Major Findings
Kato	2006	<ul style="list-style-type: none"> Twins with CWP Control twins 	1,776 41,562	Symptom-based; ACR criteria for CWP	Questionnaire assessing symptoms; standardized questionnaires; structured psychiatric interview	<ul style="list-style-type: none"> 23.4% of twins with CWP vs. 10.7% of control twins reported urinary tract problems
Kennedy	2006	<ul style="list-style-type: none"> Patients with PBS symptoms Patients with bladder pain Gynecology patients without bladder symptoms 	190 55 400	Symptom-based; Rome II criteria	Standardized questionnaires; medical history questionnaires	<ul style="list-style-type: none"> 48% of patients with bladder pain had IBS vs. 14% of those without bladder pain ($p < 0.01$) 27% of patients with bladder pain had generalized pain vs. 7% of those without bladder pain ($p < 0.01$)
Pontari	2006	<ul style="list-style-type: none"> Individuals with CP/CPPS Controls 	463 121	Symptom-based	Epidemiological questionnaire of medical history and sexual practices	<ul style="list-style-type: none"> 12.8% of individuals with CP/CPPS symptoms vs. 2.5% of controls reported a history of IBS 21.2% of individuals with CP/CPPS symptoms vs. 10.8% of controls reported a history of musculoskeletal, rheumatologic or connective tissue disease 2.2% of individuals with CP/CPPS symptoms vs. 0.8% of controls reported a history of CFS
Shaver	2006	<ul style="list-style-type: none"> FM patients Controls 	442 205	Physician diagnosis	Telephone survey assessing medical diagnoses and lifestyle behaviors; standardized questionnaires	<ul style="list-style-type: none"> 68.4% of FM patients vs. 47.2% of controls reported bladder infection
Wu	2006	<ul style="list-style-type: none"> IC patients Controls 	992 9,920	Physician diagnosis	Database analysis	<ul style="list-style-type: none"> In women, probability of IC diagnosis within 3 years after initial FM diagnosis was 0.59% if 1 episode of IC and 0.77% if multiple episodes In men, 0.08% if 1 episode and 0.09% if multiple episodes In women, probability of IC diagnosis within 3 years after initial IBS

First Author*	Year	Groups	Sample Size	Diagnostic Criteria	Study Methods	Major Findings
						diagnosis was 0.83% if 1 episode of IC and 1.14% if multiple episodes <ul style="list-style-type: none"> In men, 0.08% if 1 episode and 0.09% if multiple episodes
Wu	2006	<ul style="list-style-type: none"> IC patients Controls 	749 1,498	Physician diagnosis	Database analysis	<ul style="list-style-type: none"> 7.21% of IC patients vs. 1.47% of controls reported IBS 8.68% of IC patients vs. 3.34% of controls reported FM
Arnold	2007	<ul style="list-style-type: none"> Individuals with vulvodynia Controls 	100 325	Symptom-based	Telephone survey assessing medical and pain history, and health care use	<p>Compared to controls, women with vulvodynia symptoms were:</p> <ul style="list-style-type: none"> 2.78 times more likely to report CFS (95% CI: 1.33–6.19) 2.15 times more likely to report FM (95% CI: 1.06–4.36) 1.86 times more likely to have IBS (95% CI: 1.07–3.23)
Berger	2007	<ul style="list-style-type: none"> CP/CPPS patients Controls 	62 98	Physician diagnosis	Standardized questionnaires; manual tender point examination	<ul style="list-style-type: none"> 16.7% of CP/CPPS patients vs. 11.8% of controls had high scores on the manual tender point examination (OR = 2.64, 95% CI: 0.93–7.51, $p = 0.069$)
Kennedy	2007	<ul style="list-style-type: none"> Patients with primary vulvar disease Gynecology Control patients 	324 321	Physician diagnosis; Rome II criteria	Standardized questionnaires	<ul style="list-style-type: none"> Patients with dysplasia, vestibulitis, lichen sclerosus, lichen planus, and lichen simplex were 3–26.7 times more likely to have IBS than controls
Whitehead	2007	<ul style="list-style-type: none"> IBS patients IBD patients 	3,153 571 3,153	Physician diagnosis	Computer search of ICD-9 codes	Compared to controls, IBS patients were more likely to be diagnosed with:

First Author*	Year	Groups	Sample Size	Diagnostic Criteria	Study Methods	Major Findings
		<ul style="list-style-type: none"> Control patients 				<ul style="list-style-type: none"> Cystitis (OR: 3.6, 95% CI: 1.94–6.69) Pelvic pain (OR: 2.76, 95% CI: 2.13–3.58) Prostatitis (OR: 2.65, 95% CI: 1.70–4.10)
Araújo	2008	<ul style="list-style-type: none"> Patients with LUTS and FM Patients with LUTS without FM 	51 50	Physician diagnosis; Symptom-based	Questionnaire assessing urinary symptoms and health functioning; gynecological examination; urodynamic study; filling cystometry	<p>Compared to patients without FM, FM patients more often had:</p> <ul style="list-style-type: none"> Urge urinary incontinence (64% vs. 90.2%, $p = 0.004$) Increased urinary frequency (8% vs. 31.4%, $p = 0.007$) Detrusor overactivity (28% vs. 60.8%, $p = 0.002$)
Clemens	2008	<ul style="list-style-type: none"> IC/PBS patients Control patients 	239 717	Physician diagnosis	Computer search of ICD-9 codes	<ul style="list-style-type: none"> 1.7% of IC/PBS patients vs. 0.7% of controls had gastritis or duodenitis (OR: 12.2, $p = 0.004$) 16.3% of IC/PBS patients vs. 6.1% of controls had myalgia or myositis (OR: 3.0, $p < 0.00001$)
Dimitrakov	2008	<ul style="list-style-type: none"> CP/CPPS patients Controls 	27 29	NIDDK criteria	Standardized questionnaire; blood and urine tests	<ul style="list-style-type: none"> CP/CPPS patients averaged 2.4 comorbid disorders; 7 had CFS, FM, or arthritis; 6 had IBS

ACR = 1990 American College of Rheumatology criteria for FM, ACR criteria for CWP = American College of Rheumatology criteria for chronic widespread pain, CFS = chronic fatigue syndrome, CI = confidence interval, CP = chronic prostatitis, CPP = chronic pelvic pain, CPPS = chronic pelvic pain syndrome, CWP = chronic widespread pain, FM = fibromyalgia, IBD = inflammatory bowel disease, IBS = irritable bowel syndrome, IC = interstitial cystitis, ICD-9 = International Classification of Diseases-9, LUTS = lower urinary tract symptoms, MCS = multiple chemical sensitivity, NIH = National Institutes of Health, NIDDK = National Institute of Diabetes and Digestive and Kidney Diseases, OR = odds ratio, PBS = painful bladder syndrome, Rome I criteria = 1988 criteria for IBS, Rome II criteria = 1999 criteria for IBS.

* Please contact authors for a complete list of references.

Table 2

Overlap of symptoms and syndromes among urological and non-urological unexplained clinical conditions in studies of a single group, presented by year of publication.

First Author *	Year	Groups	Sample Size	Diagnostic Criteria	Study Methods	Major Findings
Maxton	1989	<ul style="list-style-type: none"> IBS patients 	100	Physician diagnosis; symptom-based	Interview assessing symptoms; standardized questionnaire	<ul style="list-style-type: none"> 56% reported urinary problems
Walker	1991	<ul style="list-style-type: none"> CPP patients 	137	Symptom-based	Physician diagnosis; standardized questionnaires	<ul style="list-style-type: none"> 79% had IBS symptoms
Alagiri	1997	<ul style="list-style-type: none"> Patient registry individuals with IC 	2,682	Symptom-based; patient registry	Medical history questionnaire of symptoms and syndromes	<ul style="list-style-type: none"> 30.2% reported diagnosis of IBS 37.7% reported IBS symptoms. 17.2% reported FM diagnosis 28.6% reported FM symptoms. 8.7% reported CFS diagnosis 13.8% reported CFS symptoms
Korszun	1998	<ul style="list-style-type: none"> CFS and/or FM patients 	92, of whom 42% reported TMD	ACR CDC	Questionnaire assessing prior diagnoses of psychosomatic illnesses, facial pain and TMD	<ul style="list-style-type: none"> 19% of patients with CFS and/or FM had a history of IC. 13% of patients with TMD had a history of IC.
Giamberardino	2000	<ul style="list-style-type: none"> IC patients 	2,405	NIDDK; Rome II criteria	Standardized questionnaires	<ul style="list-style-type: none"> 75% met the criteria for IBS.
Nimmuan	2001	<ul style="list-style-type: none"> Patients from Gastroenterology, gynecology, neurology, rheumatology, respiratory medicine, cardiology, and dentistry clinics 	550	Symptom-based	Questionnaire assessing various syndromes; measures of severity, sleep, and psychological complaints	<ul style="list-style-type: none"> 19% of patients with CPP symptoms had IBS symptoms 19% of patients with CPP symptoms had FM symptoms 8% of patients with CPP symptoms also had CFS symptoms

First Author*	Year	Groups	Sample Size	Diagnostic Criteria	Study Methods	Major Findings
Zondervan	2001	<ul style="list-style-type: none"> Randomly selected women from Oxfordshire Health Authority Register 	3,916	Symptom-based	Questionnaire assessing women's health issues	<ul style="list-style-type: none"> 114 women had IBS and CPP
Gordon	2003	<ul style="list-style-type: none"> Internet-savvy women who frequented vulvar pain discussion lists 	428	Symptom-based	Web-based survey	<ul style="list-style-type: none"> 34.6% reported IBS 20.6% reported FM 18.5% reported TMD 11.2% reported CF
Blanchard	2004	<ul style="list-style-type: none"> IBS patients 	196	Rome II criteria; physician diagnosis	Standardized questionnaires	<ul style="list-style-type: none"> Of 50 IBS patients, 26% reported urinary track disorders
Bernatsky	2005	<ul style="list-style-type: none"> FM patients 	180	ACR; physician diagnosis	Questionnaires assessing clinical and psychosocial variables, and health care use; standardized questionnaires	<ul style="list-style-type: none"> 36.1% reported IBS 2.2% reported CFS 1% reported irritable bladder
Williams	2005	<ul style="list-style-type: none"> CPP patients 	987	Rome I criteria	Standardized questionnaires	<ul style="list-style-type: none"> 35% met IBS criteria
Yamada	2005	<ul style="list-style-type: none"> IC patients 	30	NIDDK; ACR; physician diagnosis	Standardized questionnaires	<ul style="list-style-type: none"> 11% met FM diagnostic criteria
FitzGerald	2006	<ul style="list-style-type: none"> Patients with pain associated with urinary symptoms 	589	Symptom-based	Questionnaires	<ul style="list-style-type: none"> 30% reported IBS 18% reported CFS 9% reported FM
Hughes	2006	<ul style="list-style-type: none"> FM patients 	107	ACR	Standardized questionnaires; physical measures	<ul style="list-style-type: none"> Fatigue, pelvic pain, and physical trauma explained 23% of variance in sensory pain scores Activity level, depression, and pelvic pain explained 23% of variance in affective pain scores
Temml	2007	<ul style="list-style-type: none"> Individuals with IC symptoms 	981	Symptom-based	Standardized questionnaires	<ul style="list-style-type: none"> Women with bowel disorders had a 4.5-fold increased risk for

First Author *	Year	Groups	Sample Size	Diagnostic Criteria	Study Methods	Major Findings
Fenton	2008	<ul style="list-style-type: none">• CPP patients	175	Physician diagnosis; Rome II criteria	Questionnaires; physician examination	<div>moderate or severe IC symptoms (95% CI: 1.3–15.1, $p = 0.016$)</div> <ul style="list-style-type: none">• 35% had IC• 24% had IBS• 45% had myalgia

ACR = 1990 American College of Rheumatology criteria for fibromyalgia, CDC = 1988 Centers for Disease Control and Prevention criteria for CFS, CF = chronic fatigue, CFS = chronic fatigue syndrome, CP = chronic prostatitis, CPP = chronic pelvic pain, CPPS = chronic pelvic pain syndrome, CWP = chronic widespread pain, FM = fibromyalgia, IBS = irritable bowel syndrome, IC = interstitial cystitis, ICD-9 = International Classification of Diseases-9, NIH = National Institutes of Health, PBS = painful bladder syndrome, Rome I criteria = 1988 criteria for IBS, Rome II criteria = 1999 criteria for IBS, TMD = temporomandibular disorder.

* Please contact authors for a complete list of references.