Investigation of Clinical Characteristics of Men with Chronic Unexplained Orchialgia

by

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A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy (Nursing) in the University of Michigan 2017

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It is much more important to know what sort of a patient has a disease than what sort of a disease a patient has.

William Osler (1904), quoting Hippocrates

“…my final words to current NPs…is to take risks, chart new directions, study the results, learn from your mistakes, and enjoy change…Meliora, means ‘onward and upward’ challenging each of us to climb to his or her ‘farthest star’.”

Dr. Loretta Ford (1997)
Dedication

To my husband Len,

for always reminding me that I should “Do, or do not. There is no try.”

And to my children, Danielle, Brianna and Luke,

for demanding that I live with them in moments.
Acknowledgements

This dissertation research could not have succeeded without the support of multiple key people, and I must acknowledge my committee. This group of four very accomplished professionals was also my committee for my preliminary exam work, and they stayed with me for the dissertation research. Their support, gentle guidance, and true belief in the value of this unique project kept me going. I must acknowledge my family (including the family dog Titan), who helped to make sure I never had a shortage of highlighters, affection, emotional support or my favorite pens. My husband Len, who acted as a constant sounding board as well as my 24/7 tech support, and may have retrieved lost files...I would also like to acknowledge the support of the editorial board of the Urologic Nursing Journal, and in particular Jane Hawks, all of whom were instrumental in helping me recognize that a PhD was the appropriate and correct professional course for me. I need to acknowledge the Department of Urology at the University of Michigan Health System, many of whom acted as perpetual cheerleaders for my success in a million different tiny ways, especially as I continued to work, take classes and pursue my degree. This is especially true of Dana Ohl, Melissa Eversole and
Kandy Buckland, who supported me and allowed me to adjust my clinic days and times during four years of classwork. Lastly, I would not have survived without the near constant support of my good friend Shelley Lajiness, whose support during the final months of this project helped me see the light at the end of the tunnel.
No research project is really complete without its larger context. For me that larger context is my passion in the arena of patient care. I want to introduce you to patient of mine named Jack.

Jack was a 38-year-old gentleman who presented with his wife to my genital pain clinic. He had a history of right-sided testicular pain for over two and half years. He was initially evaluated by his primary care provider and referred to urologist. At the urologist he was prescribed multiple short courses of antibiotics, occasional narcotics, imaging studies, and more antibiotics and narcotics. None of these modalities help to address his pain, and after year he gave up; he and his wife decided to manage his pain at home as best they could. Over a year later, he re-presented with the same complaint to his primary care provider and this time was referred to my Chronic Male Genital Pain clinic. I asked about things that made his pain better or worse and the overall quality of his pain and how much interfered with his life. He reported that when his testicular pain was worse he also had hip pain and pain that radiated down his thigh to his knee. It became very clear that his pain was directly related to his work, which involved much heavy lifting,
standing, and walking. It was at times where his work was most physical that his pain was worst. He also had a bit of a paunch that probably contributed to his back strain. I discussed with Jack and his wife that my plan was a trial of anti-inflammatory medications, a non-sedating muscle relaxer, and physical therapy for his back. Jack and his wife left this clinic visit feeling their concerns had been heard, and in full agreement with the plan of care that we developed.

It has long been my goal to solve the puzzle of chronic genital pain in men, and to provide evidence for other providers to be able to do the same. This dissertation research is my first step towards that goal.
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Abstract

Chronic pain is a public health issue in the United States. Men with chronic unexplained orchialgia (CUO) are an understudied population, with significant knowledge gaps regarding to demographics, etiology, and reliable treatment. This dissertation begins to address these gaps in knowledge, within a framework that presents an organized conceptual view of this chronic pain condition. The dissertation research and interpretation of its results interpretation are guided by the Biopsychosocial Model.

This dissertation explored the feasibility of a clinic dedicated to the evaluation and management of adult men with chronic genital pain, but focused on screening for men with CUO. A total of 228 men were screened over 12.5 months; 124 reported chronic genital pain. 104 men had chronic testicular pain that had an identifiable cause; varicocele was the most common diagnosis (n = 55). 20 men had true CUO. This dedicated chronic male genital pain clinic established treatable causes for 84% of men referred for alleged CUO. This represents cost saving for men and healthcare by avoiding unnecessary surgical procedures.

The second aspect of this dissertation was a cross-sectional sample case series. All 20 men with CUO were consented; 70% (n = 14) of the men returned a survey packet
consisting of 16 standardized psychometric instruments evaluating the multidimensional nature of chronic pain. Instruments were evaluated with a sample of $n = 12$ in most cases. Demographic characteristics in the sample diverged from what has been previously reported about education and income. The median pain score was 4.00 out of 10 in the sample, with a median pain duration of 38.69 months. Men in the sample did not report urinary symptoms, depression/anxiety, or catastrophizing; instruments did not suggest a specific pain mechanism. Results showed evidence for self-reported dyscognition, fatigue and little belief in their own ability to decrease their pain. None reported a history of sexual trauma. Men reported less interference from chronic pain comorbidities in this sample than anticipated, SF-12 results conflicted with the other survey instruments, showing more impairment. This research is the first to use standardized instruments to evaluate men with CUO. Future research will include replication investigation with a larger sample.
Chapter 1

Introduction To The Problem Of Chronic Unexplained Orchialgia

Introduction

Over 116 million Americans suffer from chronic pain at a cost of over 635 billion dollars yearly in direct medical costs and decreased productivity (Institute of Medicine, 2011). Chronic pain is a current priority of the national healthcare agenda, consistent with the Healthy People 2020 (Centers for Disease Control and Prevention [CDC], 2014) to reduce the number of patients suffering from untreated pain. The Patient Protection and Affordable Care Act (Section 4305, 2010) mandated that the Secretary of Health and Human Services work with the Institute of Medicine to raise awareness of chronic pain as a public health issue.

Investigation of chronic pain is a goal of the National Pain Strategy, one that seeks to better quantify the prevalence of pain in the United States and especially in specific population groups (Interagency Pain Research Coordinating Committee [IPRCC], 2015). The National Pain Strategy embraces work designed to create baseline knowledge in understudied populations to advance and assess physical, psychological and social treatments. Because of the dynamic interaction among the biologic and
psychosocial factors that modulate an individual's description of pain and his/her potential disability, both the IOM and the National Pain Strategy Chronic acknowledge that chronic pain cannot be broken down into discrete psychosocial and physical components. The National Pain Strategy seeks to formulate strategies to address economic burdens that accompany chronic pain, especially those that prevent absence from work and dependence on medications.

This dissertation research begins to address the gap in knowledge about a specific subpopulation of understudied and underdescribed men: men with chronic unexplained orchialgia.

**Background of the Problem**

The national focus on chronic pain forms the backdrop that inspired this dissertation research to work toward clinical characterization of men with chronic unexplained orchialgia (CUO). Men living with CUO face many barriers to care, including finding a provider able to accurately evaluate their pain complaint (Quallich, 2016). Chronic unexplained orchialgia is a genital pain condition unique to men and one that lacks an evidence-based treatment algorithm. These factors contribute to men with CUO seeking evaluation and treatment from multiple providers, consistent with the behaviors of other populations with chronic pain (Hong, Corcoan, & Adams, 2009). CUO has an unknown incidence with no precedent for evaluating it as a multifactorial condition. Much remains to be learned about any underlying syndrome etiology for CUO; the natural history of CUO (i.e., how this syndrome develops and changes over time); the influence of the patient’s genetics; and biological, environmental, and lifestyle risk factors to CUO development and progression. Social and cultural factors influence
chronic pain severity and subsequent disability (Gatchel & Mayer, 2008; IOM, 2011). Physical findings alone may not provide a complete, satisfactory or holistic description for pain nor uncover potential etiologies. The Institute of Medicine acknowledges the need for a subjective conceptualization of pain that characterizes its complex evolution of biological, behavioral, environmental and societal factors in individuals (IOM, 2011).

**Statement of the Problem**

Men with CUO are evaluated in primary care, urology, neurology, physical therapy and pain clinics (Ciftci, Savas, Yeni, Verit, & Topal, 2010), and although they may represent a small number of men, the impact of their CUO on quality of life, social, sexual and economic circumstances may be substantial. A recent literature review (Quallich & Arslanian-Engoren, 2013) reveals sparse research on predictive factors that contribute to CUO or resulting rates of disability. There is also a lack of knowledge regarding reliable, non-surgical treatments (Quallich & Arslanian-Engoren, 2013). This meager literature base represents a distinct gap in the knowledge about this subpopulation of men, and contributes to a gender disparity relative to knowledge of a chronic genital pain condition in men. Undertreatment of chronic pain creates a risk for decreased quality of life, and other comorbidities such as psychosocial decline and decreased functional status (Fine, 2011). In this context, it is imperative to understand and treat men with CUO more effectively; this dissertation research works toward closing this knowledge gap through these initial steps toward clinical characterization.

This dissertation research takes the first steps to better understand CUO within a biopsychosocial model and is the first study of its kind to evaluate men with CUO standardized psychometric instruments, an approach which has proven valuable in other
chronic pain conditions. Results from this study will promote understanding of a more comprehensive approach to pain assessment and treatment for men with CUO, and may offer insight into improving assessment of psychological traits or states that influence expectations, beliefs, and the impact of chronic pain on their lives.

**Hypotheses**

This dissertation research was designed with three distinct, but progressively interrelated hypotheses. These hypotheses are designed to generate data that begins to address the gaps in knowledge and test feasibility of a method for establishing a source population of CUO for future study:

**Aim 1.** To test the feasibility of a method for identifying a source population of CUO for future study.

*Hypothesis:* Establishing a specialized clinic for men with chronic genital pain will provide a source population pool of ~30% with true chronic unexplained orchialgia at time of clinic evaluation.

**Aim 2.** To determine the feasibility of asking men with CUO to complete a lengthy survey battery of tools (some with sensitive information) to in a group of men with CUO.

*Hypothesis:* >80% of men diagnosed with true chronic unexplained orchialgia at time of clinic evaluation will fill out every survey instrument.

**Aim 3.** Obtain pilot data to inform a future study designed to fully characterize the biopsychosocial aspects of CUO.

*Hypothesis:* Men with chronic unexplained orchialgia will demonstrate comorbid symptoms associated with chronic pain.
Research Design

The dissertation research was divided into two parts. The first part was a feasibility study consisting of a convenience sample of men with male genital pain seen in an adult urology specialty clinic. These details and results are discussed in Chapter 3. The second part of the research was a pilot of a cross-sectional design using a selection of psychometric instruments to gather data exploring the multidimensional chronic pain experience of men meeting inclusion criteria; these details and results are discussed in Chapter 4. The long-term goal of exploring this subpopulation with a pilot study is to work toward the exploration of a full clinical characterization for men with CUO. Figure 1 offers a visual representation of the dissertation research.

Theoretical Approach

The theoretical model for this dissertation research drew directly from the IOM (2011) recommendations, thereby aligning it with the national chronic pain research agenda. The IOM (2011) recommended the Biopsychosocial Model (BPSM) (Engle, 1977) because this model best represents the complexity of encounters in clinical populations with chronic pain. The IOM report further recommends that research evaluating the characteristics of chronic pain place antecedents and consequences within the framework of the Biopsychosocial Model, acknowledging that chronic pain is a dynamic entity and can interfere with multiple aspects of life.

The Biopsychosocial Model

In 1977, psychiatrist George Engel published his initial proposal for the Biopsychosocial Model (Engel, 1977). This model was borne from the recognition of a need to revise both the manner in which physicians thought about patients and
approached patients. Engel discussed the need for medicine and psychiatry to acknowledge the overlap in somatic parameters and psychosocial manifestations of disease. He expressed frustration with what he described as lack of interest in the person. He saw that the pure biomedical approach, where illness was defined as physiological deviations from some normal, was failing as it tried to maintain its classic mind-body dualism, especially in the distinction between medicine and psychiatry. Engel’s model proposed a new dualism, one that advocated approaching an individual as a unique, biologic organism and as an individual within his larger social environment. The BPSM aimed to reverse the way in which medicine relegated “the psychosocial to other health professionals, such as nurses, social workers or psychologists” (Engel, 1982, p. 804). It seeks to integrate the way in which medical knowledge regarding illness and disease could be applied more individually within each clinical interaction.

The BPSM has its origins in general systems theory (Von Bertalanffy, 1968) and its approach to the interrelatedness of systems and processes; this allows inclusion of social and psychosocial conditions within a larger process for medical care. Within the BPSM, the individual is viewed as part of a hierarchy that recognizes distinct components as parts of a larger system (e.g. community) (Engel, 1982). As such, the BPSM emphasizes that a particular symptom or complaint exists within a larger context of the person’s history, experiences and sensations. The specific presentation of an individual at any given time is subject to a variety of smaller influences (e.g., social, sexual and cultural norms) within the hierarchy that might not be initially apparent (Borrell-Carrio, Suchman & Epstein, 2004)
The BPSM proposes that the interaction of biologic/physiologic, psychological, social and behavioral components creates “patiency” (Engel, 1977). It asserts that without a way to correlate biochemical abnormalities with the behavioral and psychological manifestations seen clinically, the temptation would be to circumvent symptoms and focus only “on technical procedures and laboratory measurements” (Engel, 1977, p. 132). “The biomedical model ignores both the rigor required to achieve reliability in the interview process and the necessity to analyze the meaning of the patient's report in psychological, social, and cultural as well as in anatomical, physiological, or biochemical terms” (Engel, 1977, p. 132). The social context, living environment and “the complementary system (the healthcare system) devised by society to deal with the disruptive effects of illness” (Engel, 1977, p. 132) must all be acknowledged when defining illness or health.

**BPSM and Illness**

*Disease* in the BPSM is a concept defined as a biologic condition that is disruptive, in any anatomical, pathological, physiological or psychological domains (Gatchel et al., 2007; Gatchel, McGeeary & Lippe, 2014). The concept of *illness* is defined as subjective sense of unwell, reflecting both on person and his community (Epstein et al., 2003) and symptoms may not represent the full extent of a disease. This perspective allows for causes of illness outside the individual and presents an opportunity for both the individual and the provider to acknowledge causes of illness outside the traditional constraints of the biomedical model. This also implies that situations can sustain illness, through secondary benefits (e.g. disability, increased spousal attention) or monetary gain (e.g. disability payments).
The BPSM acknowledges that individuals filter and process their experience, a perspective particularly congruent with the process of appraisal in chronic pain states. Individuals “edit” their report of their symptoms while presenting them, either to providers or in a social environment, which influences care seeking, compliance and the nature of the relationship with the provider. The result is a narrative that places their (pain) experience in a particular social context, replete with expectations about both the illness and treatment. The BPSM embraces this narrative and its representation of a larger (social) context, thereby offering insight into potential treatment approaches or avenues for success. The experience of pain is subjective and unique; the BPSM describes the integration of evidence-based approaches to care with a dynamic understanding of an individual.

The biopsychosocial approach proposes that all patients can be healed, although not necessarily cured (Epstein et al., 2003) and this may be partially through acknowledgment of their narrative and affirmation of their subjective experience by those hearing the description of their experience. This shifts the focus from a one-way physician-to-patient arrangement to a bidirectional relationship-centered model for care, incorporating social constructivism into this biopsychosocial approach to patients by acknowledging that an individual’s (pain) reality and experience are heavily influenced by social contexts (Williams, Frankel, Campbell, & Deci, 2003). The BPSM further emphasizes self-identity evaluating whether or not the patient views himself as sick or disabled as part of his initial assessment. This also requires that a provider consider the potential benefits of an individual's decision to accept his “patienthood” and his subsequent role in his own health care (Engel, 1977). Illness becomes a subjective
experience or self-attribution that disease is present (Gatchel, et al., 2007; Gatchel & Mayer, 2008), and encompasses how the individual and his support system respond to illness or disability (Gatchel, 2004).

Engel’s model (Figure 2) emphasizes the unique, subjective experience of the individual and allows researchers to identify the influence of both biological and psychosocial conditions within a dynamic framework for study (Gatchel, 2004). In 1997, Engel commented that the BPSM “provides a conceptual framework conducive to accommodating the human domain scientifically” (p. 527). The BPSM acknowledges differences in perspective and interpretation, in that some people view sensations as part of life while others identify various sensations as indicators for disease or illness.

The BPSM values an interdisciplinary approach, suggesting that failure to collaborate with other disciplines will sustain past failures that did not treat the man as a sum of his individual experiences. This approach will repeat the failures Engel first recognized in the biomedical perspective. The BPSM model is similar in nature to grand theories in nursing, in that it provides a framework for conceptualization of clinical problems and it can be easily adapted to a variety of research interests.

Alternative Model

The nursing Theory of Unpleasant Symptoms (TOUS) (Lenz, Suppe, Gift, Pugh, & Milligan, 1995) was considered as a model to ground this dissertation research. The BPSM and TOUS both acknowledge the influence of multiple factors on an individual at any point in time. The BPSM and TOUS aim to treat an individual’s experience in a complete and holistic manner. Neither the TOUS or the BPSM confine themselves to the evaluation of a single variable, symptom or condition, resulting in the potential for wide
application across a variety of disciplines. To date, the TOUS has been rarely used outside of nursing. This lack of wide adoption of the TOUS made selection of the Biopsychosocial Model for this dissertation research necessary to align this dissertation research with the national recommendations for the interdisciplinary approach to chronic pain.

Summary

Men with CUO may benefit from a comprehensive approach to pain assessment. In particular, the scores on standardized psychometric instruments may suggest a clinical presentation that is similar to other better-studied chronic pain, providing insight into more effective treatments. This new insight will promote more efficient use of healthcare resources, and prevent unnecessary trials of medical or surgical management. These goals must be closely paralleled with a reduction in bias towards this particular population, both in terms of sensitivity to health seeking behaviors in men (Hooper & Quallich, 2016) and the social and cultural stereotypes ascribed to masculinity when dealing with pain. Results from this dissertation project will also serve to close the gap in knowledge regarding this particular subpopulation of pain patients, and begin to decrease the disparity in what is known about chronic genital pain conditions in men. The results of this project can be immediately translated to advances in the clinical management of men with chronic orchialgia.
References


Figure 1. Representation of the Dissertation Research Hypotheses and Design.
Figure 2. A Conceptual Model of the Biopsychosocial Interactive Processes Involved in Health and Illness.

Chapter 2

Chronic Unexplained Orchialgia within the Context of Chronic Pain in General

Chronic pain is a current priority of the national healthcare agenda. Approximately 126 million American adults suffer from some form of chronic pain (Kennedy, Roll, Schraudner, Murphy, & McPherson, 2014). Over $635 billion is spent each year on medical care and lost productivity (IOM, 2011). Chronic unexplained orchialgia (CUO) is one of many specific chronic pain conditions. As with chronic pain in general, CUO is understudied and is poorly understood. This chapter provides a background for CUO and places what is known about CUO within the context of the larger body of literature on chronic testicular pain and chronic pain in general.

Integrative Review of the Chronic Testicular Pain Literature

Chronic pain is a complex and difficult clinical symptom for clinicians to understand because of its personal nature and an individual’s subjective perception and past experiences (Gatchel, Peng, Peters, Fuchs, & Turk, 2007; Tait & Chibnall, 2014; Turk & Melzack, 2011). A recently published integrative literature review spanning January 1970-September 30, 2012, demonstrated the sparse body of research knowledge available discussing the clinical presentation of men with CUO (Quallieh &
& Arslanian Engoren, 2013; Appendix A). Results of the literature review support the need for an investigation into men with CUO that includes parameters such as “its impact on daily activities, any disability related to pain, an account of utilization of services, and the costs of pain and pain care” (p. 402, Quallich & Arslanian-Engoren, 2013). The scarcity of this information in papers published prior to 2013 highlights the lack of information on which to base our understanding of men with CUO.

Since publication of this integrative review, only six publications met the inclusion criteria of the original integrative literature review (Cassidy, 2015; Cui & Terlecki, 2016; Khambati, Lau, Gordon, & Jarvi, 2014; Marconi, et al., 2015; Najari, Robinson, Paget, & Paduch, 2014; Parekattil, Gudeoglu, Brahmbhatt, Priola, Vieweg, & Allan, 2013). Of these six papers, four are research papers (Table 1) and two are case review papers (Table 2) investigating treatment and management for adult men with CUO. Consistent with observations in the Quallich and Arslanian-Engoren (2013) review of the literature, these new papers include sparse information about demographics, pain characteristics or site of pain. These recent published papers continue the focus on surgical treatment (such as spermatic cord denervation) for the unexplained orchialgia, adding little the understanding of the CUO population.

Chronic Pain

The Interagency Pain Research Coordinating Committee (IPRCC) was developed in 2011 by the Department of Health and Human Services to organize pain research and activities. The task of the IPRCC is to identify critical gaps in basic and clinical research on symptoms and causes of pain and support population-based research regarding the incidence and prevalence of chronic pain. The IPRCC encourages population-based
research to help reduce pain and remediate treatment disparities among subgroups, based on dimensions, such as gender or socioeconomic status. In 2011, after its creation, the IRPCC adopted the Institute of Medicine’s 2011 report and its recommendations, which proposed avenues for addressing chronic pain as a public health issue.

This Institute of Medicine (IOM) 2011 document titled “Relieving Pain in America” includes specific recommendations a) for the assessment of chronic pain, b) for pain evaluation in previously understudied populations, and for the education of providers at all levels. The IOM report further recommends that future research evaluating antecedents and consequences of chronic pain place these characteristics within the framework of the Biopsychosocial Model (Engel, 1977) (ref), emphasizing the subjective experience of the individual, and allowing researchers to place the influence of biological and psychosocial conditions within a framework for study. The report concludes that the cost of chronic pain is so significant, in terms of healthcare dollars and social consequences, that additional study is imperative. The IPRCC recently reinforced the IOM’s recommendations when issuing the National Pain Strategy to work toward an evidence-based, culturally sensitive prevention and care algorithm (IPRCC, 2015).

Comorbid and Allied Pain Conditions

From a utilitarian perspective, the most basic function of acute pain is to command one's attention to possible injury that might threaten survival. In the absence of acute tissue damage or injury, such as with chronic pain, prolonged pain is largely maladaptive. Chronic pain impacts many domains, not solely psychological or physical ones (IOM, 2011; Jensen & Turk, 2014; Molton & Terrill, 2014). Full description of the illness burden with chronic pain is complex, and must acknowledge age-related
differences. Fine (2011) reviewed numerous studies that reported the negative impact that pain has on multiple domains, including

- Quality of life;
- Functional capacity/limited activity;
- Fatigue;
- Sleep disturbance/sleep deprivation;
- Mood (depression/anxiety/anger);
- Dyscognition (memory/attention);
- Coping mechanisms;
- Gender-specific issues, such as sexual function.

This review (Fine, 2011) demonstrated a lack of association between chronic pain and sexual function, although the individual comorbidities listed can each impact sexual function.

Since Fine’s 2011 review, the relationship of chronic pain with mood has been investigated. Pain itself provokes an emotional response; it is this unique reaction that sets the stage for treatment successes and failures, as well as potential disability (Watson & Kendall, 2013). Pain is an independent risk factor for depression; depression, is both a normal reaction to pain and decreased activity, but can also become pathologic in chronic pain states (Watson & Kendall, 2013). A recent review of modulation of pain by cognitive and emotional states shows positive or negative moods and expectations can influence treatment outcomes and decrease or increase reports of pain (Busnell, Ceko & Low, 2013). Gatchel et al. (2007) performed an extensive review of experimental models of pain, and reviewed the role of emotions from a “sensory-discriminative, cognitive-
evaluative, and motivational” (p. 598) perspective. These authors note multiple studies linking emotional states to chronic pain, suggesting that pain and emotions interact in a variety of ways to promote and sustain its comorbid symptoms. For example, anxiety has been implicated in increased affective pain responses and maladaptive pain behaviors because it represents uncertainty about the future and uncertainty about the meaning of the pain (Gatchel et al., 2007). Lumley et al. (2011) reviewed the literature on pain and emotion from 2000-2010. They reported that pain-related anxiety can result in avoidance of activities that promote recovery and may have a role in amplification of somatosensory input. Psychological and social beliefs and behaviors can create and perpetuate maladaptive coping, such as childhood traumatic events having a role in some pain conditions (Lumley et al., 2011). Two other recent reviews (Jensen & Turk, 2014; Molton & Terrill, 2014) offer evidence that pain behaviors alone can sustain pain, and create disability that is not a function of the pain itself, such as a lack of movement leading to muscle weakness.

**Gender Gap Regarding a Chronic Genital Pain Condition**

In the first section of their extensive systematic literature review, Racine et al. (2012a) reported 10 years of published data demonstrated that experimental pain testing failed to establish a consistent pattern of differences between men and women. These authors concluded that published study results ($n = 122$) were heavily influenced by both the outcome measures (e.g. time exposed to painful stimulus, site of body tested) chosen by researchers and the pain modalities tested (e.g. pressure pain, ischemic pain, electrical pain). This has unclear implications clinically, as these results were based on controlled experimental conditions. This same group of authors also reviewed published studies
(n = 128) examining regarding possible biopsychosocial factors in pain sensitivity between men and women (Racine et al., 2012b). The review reported that anxiety was a stronger predictor of pain in men, and may have an increased effect on pain perception in males. Racine et al. (2012b) also stated that distraction may be an efficient coping style for men faced with pain. Gender expectations seem to have a role in pain perceptions in experimental settings, but again this is an unclear relationship to clinical presentation and symptom report. Racine et al. (2012b) concluded that current data is insufficient to establish a true influence from biopsychosocial factors or to explain differences in pain perception between men and women. Gender differences in pain intensity and pain perception, as this manifests clinically, remain poorly described and poorly understood. This is despite clear gender differences in prevalence for some types of chronic pain, such as fibromyalgia, leading to speculation that there are gender differences in pain perception although to date evidence for this is inconclusive.

El-Shormilisy, Strong, and Meredith (2015) performed a systematic review with strict inclusion criteria (adult patients, pain >3 months, measure coping/pain management strategies, measure function) for reporting gender-specific outcomes when evaluating adults with chronic nonmalignant pain. These authors reported that in the seven papers that met inclusion criteria, results demonstrated that men catastrophize more when in pain, and manifested increased anxiety, leading to increased interference from pain during daily functions (return to work or as measured on a pain interference scale). They concluded that gender-specific coping styles influenced functional status in men and women with nonmalignant chronic pain and confirmed the complex association of chronic pain with depression and anxiety (El-Shormilisy, Strong & Meredith, 2015).
Keogh (2015), in recent selective review that examined general themes in published men’s health literature, reported that men have a lower use of pain services and lower use of analgesics than women. Keogh (2015) suggests one’s understanding of men with chronic pain can be strengthened by incorporating a men’s health view, one that incorporates acknowledgement of current psychosocial stereotypes about men and pain. Furthermore, men may be using avoidance by seeking multiple evaluations when they experience chronic pain, as they continue to pursue an explanation and diagnosis that is consistent with their masculine self-schema (minimizing symptoms to the point of insignificance, as interest in health or their bodies can be interpreted as “feminizing”) rather than accepting the diagnosis of “pain” (Wenger, 2011; Hooper & Quallich, 2016).

Vulvodynia is a chronic genital pain condition in women and ongoing research seeks to evaluate the underlying pain mechanisms while combining specific physiologic and psychological interventions (Cox & Neville, 2012; Zhang et al., 2011). Standard evaluation of women with a chronic genital pain condition, such as vulvodynia, follows a process that includes questioning the woman about the personal meaning and attributes of her pain and its meaning in the context of her sexual function (Bergeron, 2011; Fall et al., 2010; Haefner et al., 2005; Johansen & Weidner, 2002; Reed et al., 2014). This represented a paradigm shift toward understanding this condition as multifactorial. This shift recognized the subjective nature of pain and the interplay of biological psychological and social factors that contribute to and sustain an illness experience (Bergeron, 2011) such as the relationship of the perceptions of their femininity and a desire for validation of their pain.

**The Intersection of Chronic Pain and Sexuality**
Chronic pain affects an individual’s well-being and quality of life (Gatchel et al., 2014; Jensen & Turk, 2014) and likely influences sexuality. Certain types of chronic pain, particularly chronic pelvic or genital pain, might also have direct effects on sexuality, and may reflect a specific aspect of the contribution of chronic pain to “disordered social relations” (Jensen & Turk, 2014, p.108). One’s conceptualization of sexuality is a direct influence of factors such as class, gender, and education, demonstrating the inextricable relationship between biology and the cultural reality of sexual behavior (Gagnon, 1975; Quallich, 2014).

Much of the groundwork examining the relationship between chronic pain and sexuality is reported with chronic back pain patients (Maruta & Osborne, 1978; Osborne & Maruta, 1980; Sjogren & Fugl-Meyer, 1981; Vander Kolk, Chubon & Vander Kolk, 1992; Monga, Tan, Osterman, Monga, & Grabois, 1998). A retrospective study by Vander Kolk et al., (1992) reported that 72% of their cohort of male and female patients with back injuries (n = 100) reported some degree of sexual dysfunction, determined by a decrease in the frequency of sexual activity, with a mean reduction of 71.82%. Only a small relationship was reported between pain level and reduction in frequency of intercourse, suggesting that other unmeasured variables impact sexual activity. Others have reported that subjects describe decreased sexual satisfaction at the initial onset of their pain (Sjogren & Fugl-Meyer, 1981).

In a predominantly male veteran sample, Monga et al. (1998) found men (n = 62) and women (n = 8) with chronic pain in a variety of sites (e.g. back, legs, shoulders, genitals) experienced difficulties with sexual arousal, sexual behavior, climax, and sexual relationships, but not sexual fantasy. These authors reported that patients with pain may
be too distracted by their chronic pain to reach a sufficiently high level of sexual arousal, and that greater sexual dysfunction is associated with less successful coping mechanisms (e.g. catastrophizing, perceptions of decreased control, fear of pain). In this convenience sample, Monga et al. (1998) showed that patients who had positive control appraisals for both pain and life domains had higher scores on the sexual functioning scales, while patients who were employed had overall better sexual function and libido than those receiving disability payments.

Ambler, de C. Williams, Hill, Gunary, and Cratchley (2001) reported that in their sample of men and women ($n = 237$) that pain had a negative impact on sexual function for most patients, independent of mood. Their sample had a low incidence of depression (measured on the Hospital Anxiety and Depression Scale) despite pain with sexual position and sexual performance concerns. Kwan, Roberts and Swalm (2005) suggested chronic pain impacts sexual activity, but this does not imply a lack of satisfaction with sexual activity. Kwan, Roberts and Swalm (2005) incorporated a mixed methods approach (prospective survey with retrospective chart review) to survey 151 men and women with a variety of nonmalignant chronic pain conditions. Their results offered evidence that men and women with chronic pain were highly adaptive, altering their approach to sexual activity based on physical limitations, and that satisfying sexual activity depended more on personal relationships and social support than successful resolution of all pain. These authors reported that as study participants’ health circumstances changed, their perspective on sexual activity and intimacy also changed, with sexual activity becoming less important overall to quality of life than comorbid domains such as sleep and activities of daily living.
In a small series \( (n = 3) \) Arabkheradmand et al., (2008) reported that chronic pain and altered erectile dysfunction often coexisted, but that erectile difficulties were not commonly treated in the context of chronic pain. Men were age 25, 65, and 47; no mention was made of ethnicity. All three men suffered a traumatic injury that resulted in chronic pain and sexual function complaints. Results demonstrated that treating erectile difficulties improved overall pain scores and alleviated psychological symptoms.

Ruehlman, Karoly and Taylor (2008) reported that in a national US sample of 2071 men and women aged 25 to 80 with chronic pain, 37% reported no interference with sexual functioning. In the men belief in a cure was a predictor of increased interference with sexual functioning and may be related to treatment-seeking. Regression analysis of the results revealed that catastrophizing was a predictor of pain interference \( (b = .234) \) on sexual function for both men and women. Their findings are consistent with the scant body of previous research demonstrating men who seek treatment for their pain report higher levels of disability across domains, including sexual function. This study did not clarify whether it is alterations in sexual function or pain itself that drives men to seek treatment, and conclude that “the link between gender, pain’s perceived interference with sexual activity, and treatment seeking merits further empirical scrutiny” (p. 134).

**Sexuality and Chronic Unexplained Orchialgia**

Only two papers to date (Ciftci et al., 2011; Lutz et al., 2005) have discussed the impact of chronic testicular pain on sexual function. Lutz et al. (2005) reported on a longitudinal sample of 1,248 Caucasian men (median age 60, range 40-79) residing in Olmsted County, Minnesota, with a regular sexual partner. Five sexual function domains (libido, erectile function, ejaculatory function, problems with sexual function, overall
satisfaction) were assessed. Results demonstrated that the focal nature of testicular pain had a greater negative impact on the sexual function domain than with other domains. Although the association between generalized urogenital pain and sexual function was unclear, there was an association between testicular pain and decreased libido.

More recently, Ciftci et al. (2011) conducted a descriptive study using a small sample of 50 men with orchialgia and 50 controls using the International Index of Erectile Function (IIEF). No significant difference in IIEF scores between groups for overall erectile function was noted (total score controls = 48.7 ± 12.10; total score men with testicular pain = 46.0 ± 10.9). Men with orchialgia reported decreased libido (score 2.90 ± 1.4; controls 3.76 ± 2.2) and decreased satisfaction (score 2.94 ± 1.4; controls 3.50 ± 2.7) related to current sexual activity. Men with orchialgia also reported an overall lower quality of life score measured by the World Health Organization Quality of Life Questionnaire (9.7 ± 2.8 [range 0-12]) when compared with controls (6.8 ± 3.1). This suggests chronic testicular pain impacts both daily activities and overall quality of life. This study did not investigate other comorbid pain conditions that influence libido, such as depression or fatigue. Chronic pain may not change all aspects of male sexuality, but a genitourinary location may have a particularly profound impact both on function and on well-being.

Overview of Chronic Unexplained Orchialgia

Adult men with chronic orchialgia or chronic testicular pain are evaluated in primary care, urology (Ciftci, Savas, Yeni, Verit, & Topal, 2010) and pain clinics. Chronic unexplained orchialgia represents a challenging clinical entity for providers to successfully treat and manage because of its presently unclear etiology. There can be
straightforward explanations for seemingly chronic unexplained orchialgia (varicocele or referred pain from an inguinal hernia), but often the etiology remains unexplained. In fact, from 18.6% (Cifti et al., 2010) to 25% (Davis, Noble, Weigel, Foret, & Mebust, 1990) of chronic orchialgia has no known cause, despite extensive evaluation.

The three most often cited studies regarding chronic testicular pain (Costabile, Hahn, & McLeod, 1991; Davis et al., 1990; Schover, 1990) are over 25 years old and consist of a combination of retrospective and prospective chart review or interview (Schover, 1990), without inclusion of standardized psychometric tools. The history of sexual trauma reported in the Schover has never been substantiated or investigated in subsequent studies. The methodological limitation of these studies of chronic orchialgia provide only a sparse representation of the men with this condition and lack key details, such as pain comorbidities, quality of life or pattern of pain, to aid our understanding of this important men’s health condition. Past studies of CUO have focused on the success of invasive procedures without the inclusion of a control group, and serve as an example of the biomedical model proceeding without inclusion of psychosocial aspects, as noted in a recent integrative literature review (Quallich & Arslanian-Engoren, 2013). These same studies fail to report physical examination details, often resulting to the term “scrotal contents pain” in place of distinguishing among scrotal structures.

The lack of rigorous studies threatens the external validity of currently proposed treatment algorithms or recommendations for treatment, and compromises the ability to predict or describe a phenotype for chronic orchialgia. Published studies do not routinely report demographic information except age, limiting the generalizability to other socioeconomic groups. The studies are commonly single-center, limiting generalizability
to other countries or geographic areas. With the exception of visual analogue scales, previous studies have not included standardized assessment instruments, citing the rationale that there are no tools or instruments specific to, or validated in, this subgroup of men (Benson & Levine, 2012). The current algorithm (Levine & Hoeh, 2015) for assessment and treatment of CUO minimizes psychosocial assessment in favor of surgical or medical intervention and is designed from only a urology perspective.

The lack of rigorous evaluation of CUO in the literature closely parallels the history of interstitial cystitis (IC) and other urologic chronic pelvic pain syndromes (UCPPS), which until recently were evaluated from only a urology perspective, resulting in a record of unpredictable results and poor treatment success (Clemens, 2014). The shift in focus, due to large epidemiological studies (Multidisciplinary Approach to the Study of Chronic Pelvic Pain [MAPP], pointed toward the possibility of an underlying chronic pain syndrome in patients with UCPPS (Krieger, et al., 2015). Treating UCPPS from only the urology perspective did not take into account the multifactorial nature of what eventually would be identified as a chronic pain, not urologic, condition. A shift in focus from a strictly urology component of UCPPS included related disciplines (basic scientists, epidemiologists, pain specialists, neuroimaging, translational animal models) and refocused the investigation into the etiology of UCPPS, allowing for potential systemic syndromes that may have a relationship with UCPPS. Exploration of UCPPS through application of the principles of chronic pain resulted in progress toward identification of characteristics that UCPPS patients shared with other chronic pain populations. Two phenotypes of UCPPS patients have been identified, one with bladder-
focused symptoms and one with more systemic, centralized pain (Clemens, 2014; Griffith et al., 2016; Krieger et al., 2015).

There is no analogous literature base to allow comparison between men with CUO and other chronic pain groups. The only Cochrane review that discusses nonsurgical options for the treatment of chronic pelvic pain limits its discussion to options for women only (Cheong, Smotra, & Williams, 2014). Previous literature has failed to establish rigorous inclusion criteria that establishes testicular pain as truly localized and the only site of pain among study participants. As a result, authors reporting study participants with “testicular pain” may in fact have pain to any of the scrotal contents (e.g. testis, spermatic cord, epididymis, or the scrotal skin itself). This clouds the ability of clinicians to determine success and compare outcomes among reported interventions.

Consistent failure to find a relationship between organic pathology and the reports of pain has fostered the belief that there is a psychologic component to CUO or that this condition represents a subtype of a “pain prone” population (Costabile et al. 1991). Conclusions about the true significance of CUO as a condition affecting men is limited by the lack of data reporting incidence, and this is influenced by the fact that there was not an individual ICD-9 code specific to this diagnosis (Quallich, & Arslanian-Engoren, 2014). This lack of knowledge has contributed to stigmatization of men with CUO, and research has neglected specific considerations that may address the unique needs of this male population.

Previous Attempts to Categorize Chronic Orchialgia
Pain that has been anatomically localized to the testis(es) has been described by a variety of concepts in the literature (Table 3). The name chosen to describe any condition can have significant implications, in the minds of providers, in the minds patients themselves and in the minds of the public and stakeholders. Including “pain” in the title implies that there is urgency for treatment. For clinicians who are familiar with the concepts used when treating chronic pain it also implies a multidimensional aspect to a patient's experience, as anticipated by the Biopsychosocial Model.

The International Association for the Study of Pain (IASP, 2011) and European Association of Urology (EAU) (Fall et al., 2010) guidelines (Table 3) include urinary and sexual function in men with chronic genital pain. The sparse literature on CUO does not reflect the presence of either lower urinary tract or sexual dysfunction (Quallich, & Arslanian-Engoren, 2013), calling into question any attempt to link chronic testicular pain with other urologic pain syndromes in men.

The Need for a Concept Analysis

A concept analysis was vital to progression of the understanding of CUO, and was completed as independent study prior to the dissertation project (Quallich, & Arslanian-Engoren, 2014). This allowed for the development of an initial conceptual definition for a phenomenon of interest. Chronic unexplained orchialgia needed a conceptual reexamination, one that was consistent with contemporary concepts about the multidimensional nature of chronic pain and its effects on daily life. Guided by Walker and Avant (2011), this concept analysis was conducted to clarify the concept for further study and distinguish CUO from other similar conditions.
The need for a concept analysis was vital; there was no individual ICD-9 code for chronic orchialgia, making a true estimation of its incidence and prevalence challenging despite the sophisticated data tracking offered by contemporary electronic medical records (EMR). Papers have been published using a variety of terms, making comparisons among them difficult, and highlighting the challenges in successfully identifying the true nature of the CUO condition. The concept analysis provided a method to establish a solid conceptualization for CUO, and clarify the concept while providing a succinct definition that included its key attributes from the literature.

A definition that reflects the complexity and individual nature of the chronic pain experience was developed: “Chronic unexplained orchialgia is a subjective negative experience of adult men, perceived as intermittent or continuous pain of variable intensity, present at least three months, localizing to the testis(es) in the absence of objective organic findings, that interferes with quality of life” (Quallich, & Arslanian-Engoren, 2014, p. 1724).

Model Case as Illustrative Sample of Focus for This Dissertation

A model case offers an exemplar of a particular phenomenon while demonstrating its defining attributes (Walker & Avant, 2011). The following is a model case for chronic unexplained orchialgia:

JS is a 43 year old Caucasian male presenting to Adult Urology clinic with complaints of chronic orchialgia lasting 32 months. His history is notable for spontaneous onset of right testicular pain while cooking at home with his wife. There is no history of genital trauma, infection or low back injury, and he has no urinary symptoms. Previous visits to five different specialty providers, three of which were urologists, did not offer an explanation for his pain. He was offered a variety of medications, including non-steroidal anti-inflammatories, gabapentin, and tramadol, all resulting in little relief. The pain waxes and wanes independent of activity, position or rest. This pain has prevented him from pursuing his hobby of kayaking, decreased his productivity as an information technologies manager,
and limited his time as a middle school track coach. JS has undergone serial physical examinations and scrotal ultrasounds that have consistently been normal, and spermatic cord blocks have provided only a few hours’ relief. To date, no explanation for his pain has been identified.

Summary

In general, the current state of the science regarding CUO is underdeveloped and incomplete. This represents both a gender gap and a disparity in the knowledge of this subpopulation of men with chronic pain. At the time of the 2013 integrative literature review, “chronic testicular pain” was chosen to describe this condition (Quallich, & Arslanian-Engoren, 2013). However, the 2014 concept analysis revealed that “orchialgia” was a more prevalent term in published literature, and “chronic unexplained orchialgia” now represents the phenomenon of interest (Quallich, & Arslanian-Engoren, 2014).

This dissertation research is consistent with both the IOM 2011 report and the subsequent National Pain Strategy (NPS) (Mackey, 2014) that urge clinicians and researchers to focus on disparities in pain care. In this dissertation project, the specific disparity of interest is men with “high impact chronic pain” that is “associated with substantial restriction of participation in work, social and self-care activities for six months or more” (p. 9) as described by the IPRCC (2015). This study establishes groundwork to understand CUO within a biopsychosocial model, and is the first study of its kind to evaluate men with chronic orchialgia with a rigorous approach using a combination of legacy instruments and newer psychometric instruments.

The purpose of this dissertation research is to begin to address the gap in knowledge about a very precise subpopulation of men, one for whom there is a health disparity as regards chronic pain, specifically CUO. The long-term goal of this research trajectory is to promote a more comprehensive approach to pain assessment and treatment.
for this subset of men, and offer insight into improving assessment of psychological traits or states that influence expectations, beliefs, and thoughts about the chronic pain that they experience and its impact in their lives. These insights have the potential for translation into future prevention and treatment strategies for men with CUO.
References


<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Country</th>
<th>n</th>
<th>Age Range (mean)</th>
<th>Methods</th>
<th>Standardized tools</th>
<th>Pain Characteristics</th>
<th>Duration (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parekattil, et al. (2013)</td>
<td>US</td>
<td>29</td>
<td>16-70 (44)</td>
<td>Prospective study; examination of spermatic cord biopsies after microsurgical denervation of spermatic cord</td>
<td>Spermatic cord biopsies</td>
<td>Described 6 patterns of pain location and radiation in study participants</td>
<td>&gt; 3 mos</td>
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<tr>
<td>Khanbati, et al. (2014)</td>
<td>Canada</td>
<td>18</td>
<td>(44)</td>
<td>Pilot open label study of OnabotulinumtoxinA (Botox®) spermatic cord block</td>
<td>Chronic Ecidymitits Symptom Index (CESI) Visual Analog Pain Scale (VAS) (0-10)</td>
<td>VAS before treatment 7.36 After treatment 5.61</td>
<td>&gt; 51 mos</td>
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<td>Marconi, et al. (2015)</td>
<td>Chile and Germany</td>
<td>35</td>
<td>18-70 (50)</td>
<td>Prospective study of microsurgical denervation of spermatic cord</td>
<td>Visual Analog Pain Scale (VAS) (0-10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cui &amp; Terlecki (2016)</td>
<td>US</td>
<td>95</td>
<td>20-69</td>
<td>Retrospective chart review evaluating B12 and testosterone levels</td>
<td>Serum Testosterone level Serum B12 level</td>
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</tr>
</tbody>
</table>

* Not clear that all testicular pain was unexplained.
Table 2

*Case Studies/Series Evaluating Chronic Testicular Pain Since 2013 Integrative Literature Review*

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>n</th>
<th>Age(s)*</th>
<th>Standardized tools</th>
<th>Pain Characteristics</th>
<th>Duration (mos)</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>USA</td>
<td>Bilateral testis</td>
<td></td>
<td>&gt;24 mos</td>
</tr>
<tr>
<td>Najari et al. (2014)</td>
<td>1</td>
<td>37</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cassidy (2015)</td>
<td>9</td>
<td>41.8 (range 25-73)</td>
<td>Visual analog scale</td>
<td></td>
<td>&gt;3 mos</td>
</tr>
<tr>
<td>Canada</td>
<td></td>
<td></td>
<td>7.7 (range 5-8.5 preoperatively)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>0.3 (range 0-2 postoperatively)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*No other demographic information reported.*
<table>
<thead>
<tr>
<th>Organization or Author</th>
<th>Year</th>
<th>Term or Syndrome</th>
<th>Definition</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Davis et al.</td>
<td>1991</td>
<td>Chronic orchialgia</td>
<td>Intermittent or constant unilateral or bilateral testicular pain three months or longer in duration that significantly interferes with the daily activities of a patient so as to prompt him to seek medical attention (p.936)</td>
<td>Localizes pain specifically to testis(es) Does not address the multiple potential domains affected by chronic pain</td>
</tr>
<tr>
<td>Levine</td>
<td>2010</td>
<td>Chronic scrotal contents pain</td>
<td>Chronic pain that occurs in any portion of the scrotum or its contents (p. 209)</td>
<td>Neglects differences in structure, function, or innervation of scrotal contents Does not address the multiple potential domains affected by chronic pain</td>
</tr>
<tr>
<td>European Association of Urology (EAU)</td>
<td>2010</td>
<td>Scrotal pain syndrome</td>
<td>Persistent or recurrent episodic scrotal pain associated with symptoms suggestive of urinary tract or sexual dysfunction No proven epididymoorchitis or other obvious pathology</td>
<td>Part of EAU chronic pelvic pain guidelines Includes chronic testicular pain Guidelines acknowledge the possible role of the pelvic floor as a contributor Does not address the multiple domains affected by chronic pain</td>
</tr>
<tr>
<td>International Association for the Study of Pain (IASP)</td>
<td>2011</td>
<td>Scrotal pain syndrome</td>
<td>Occurrence of persistent or recurrent episodic pain localized within the organs of the scrotum that may be associated with symptoms suggestive of urinary tract or sexual dysfunction No proven infection or other obvious local pathology Often associated with negative cognitive, behavioral, sexual, or emotional consequences as well</td>
<td>Part of IASP Taxonomy project</td>
</tr>
</tbody>
</table>
International Association for the Study of Pain (IASP) 2011

**Testicular pain syndrome**

Occurrence of persistent or recurrent episodic pain perceived in the testis/testes and may be associated with symptoms suggestive of urinary tract or sexual dysfunction

No proven infection or other obvious local pathology

Often associated with negative cognitive, behavioral, sexual or emotional consequences as well as with symptoms suggestive of lower urinary tract and sexual dysfunction

Previous terms have included orchitis, orchalgia, and orchiodynia; these terms are no longer recommended

Part of IASP Taxonomy project

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International Association for the Study of Pain (IASP) 2011

**Epididymal pain syndrome**

Occurrence of persistent or recurrent episodic pain perceived in the epididymis that may be associated with symptoms suggestive of urinary tract or sexual dysfunction

No proven infection or other obvious local pathology

Often associated with negative cognitive, behavioral, sexual, or emotional consequences as well as with symptoms suggestive of lower urinary tract and sexual dysfunction

Part of IASP Taxonomy project

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Chapter 3

Feasibility Testing of a Male Chronic Genital Pain Clinic to Identify Men with 
Chronic Unexplained Orchialgia

Introduction

This study aimed to test the feasibility of a dedicated clinic for the evaluation of 
men with chronic male genital pain to address two patient care concerns. First, men with 
chronic genital pain complaints are perceived as challenging patients. Men with chronic genital pain scheduled can be disruptive within the normal pace of a clinic, as they 
commonly present with an extensive medical history and records from multiple prior 
providers and unclear treatment options. Second, the number of men with CUO were not 
captured clearly by ICD-9 codes. Furthermore, men with CUO are scattered amongst 
providers, making them a difficult group to identify for study. In the primary 
investigator’s practice setting, identifying men with chronic orchialgia would mean 
reviewing the daily schedules of several providers and traveling to any of eight clinic 
sites within the same healthcare system where men might be scheduled in order to 
approach them to participate in a research study. Therefore, the principle investigator 
embarked on a feasibility study to determine the practicality of establishing a small
subspecialty clinic within the urology department where she practiced. This subspecialty clinic would be dedicated exclusively to men with chronic genital pain patients, accepting referrals and managing follow-up care. In order to capture the greatest number of potentially appropriate referrals for the subsequent CUO study, this clinic was designated the “Chronic Male Genital Pain” clinic.

**Hypothesis**

This research was designed to generate data that begins to address the gaps in knowledge and test feasibility of a method for establishing a source population of men with chronic unexplained orchialgia for future study, from within a larger population of men with chronic genital pain.

Aim 1. To test the feasibility of a method for identifying a source population of CUO for future study.

_Hypothesis:_ Establishing a specialized clinic for men with chronic genital pain will provide a source population pool of ~30% with true chronic unexplained orchialgia at time of clinic evaluation.

**Methods**

**Design**

This was a feasibility study consisting of a convenience sample of men with male genital pain seen in an adult urology specialty clinic. The timeframe for the study was projected to be a year, which was deemed adequate for estimating feasibility of a clinic long-term. Because of the unclear number of referrals for chronic male genital pain to the urology department, coupled with the inability to accurately capture the number of these
men that previously seen due to nonspecific ICD-9 coding, there was not a way to estimate the number of men that were anticipated as referrals.

**Procedures**

Because of the principle investigator’s existing practice within the urology department at a large academic health system (UMHS), this new clinic had the advantage of not requiring additional clinic space or additional support staff. Nevertheless, setting up this specific subspecialty clinic required a multi-step process involving many system and infrastructure steps (Appendix B). In brief, the clinic was initially opened every other Tuesday, beginning mid-June 2015. This “best guess” scheduling was designed to accommodate the lack of clarity regarding the true number of men with chronic genital pain evaluated by the department and the anecdotal consensus that it was “a fair amount”. Ongoing evaluation and adjustments to the schedule were anticipated to ensure men were scheduled appropriately (e.g., the clinic was not used to schedule infertility patients or vasectomy consults) and to accommodate increasing number of referrals, as needed. Based on the principle investigator’s previous experience with the complexity of patients of this type, coupled with the fact that UMHS is a tertiary referral center, new patient appointments were set at 45 minutes.

Referral criteria were designed (Table 4) for the “Chronic Male Genital Pain Clinic”, including consult request guidelines that would be available to referring providers outside the University of Michigan Health System (UMHS). Expert opinion and the best available evidence from the literature formed the basis for these guidelines that directed the preliminary workup of men with chronic genital pain prior to referral to the clinic. Referral criteria suggested that men have a scrotal ultrasound within the
previous 3 to 6 months prior to referral, to ensure that men who needed urgent evaluation for testicular cancer were not inadvertently scheduled into this clinic. The absence of this imaging study did not preclude scheduling into the clinic.

To capture the maximum number of referrals for chronic male genital pain, the principle investigator reviewed the diagnoses lists for each adult urology provider by hand, to determine which providers were seeing patients appropriate for referral into the new clinic. The next step was for the principle investigator to contact the providers who accepted these diagnoses (testicular pain, scrotal pain, penis pain, groin pain, or epididymal pain > 3 months) to ask if they would be willing to allow this alteration in scheduling, meaning these referrals would automatically be scheduled into the new clinic. Finally, the scheduling staff were instructed to contact the principle investigator directly with any questions about scheduling referrals for male genital pain that originated in the community or from within UMHS.

These steps of referring men into the clinic were considered as “primary screening” for the purposes of this feasibility study. The inclusion/exclusion criteria described in Chapter 4 were considered “secondary screening” for the purposes of specifically identifying amongst the men referred for chronic male genital pain those meeting criteria for the Chronic Unexplained Orchialgia (CUO) research.

**Inclusion Criteria for Primary Screening.**

The inclusion criteria for the Chronic Male Genital Pain clinic are as follow: men over age 18, have genital pain for more than 3 months, and be willing to be evaluated in this specialized clinic. The following definition developed after a recent concept analysis (Quallich, & Arslanian-Engoren, 2014) was used to guide evaluation of men with
potential CUO: “a subjective negative experience of adult men, perceived as intermittent or continuous pain of variable intensity, present at least three months, localizing to the testis(es) in the absence of objective organic findings, that interferes with quality of life” (p. 1724).

**Exclusion Criteria for Primary Screening.**

Men were excluded from primary screening at the clinic if they reported chronic non-genital pain (including chronic pelvic pain), acute genital pain or other urologic complaints. No adult men were excluded from referrals nor from the overall feasibility study based on their status as part of a minority group or subgroup. No specific attempts at recruitment of minority groups was made. Sexual orientation (queried on the history and physical form) or previous evaluation in a urology clinic or pain clinic did not exclude men from participating.

**Results**

Based on informal discussions with the principle investigator, support of this new clinic among urology providers and clinical staff was unanimous. No providers wished to retain referrals for chronic male genital pain. By number, the providers were urologists (n = 8), family practice physicians paired with the urology department (n = 3), and urology advance practice providers (n = 3) listed as accepting men with complaints of chronic male genital pain diagnoses (although frequently men were scheduled into available openings with providers not formally identified as accepting these diagnoses).

Initial referrals were from within the urology department and other UMHS providers and few from urologists and primary care providers outside UMHS. Referral
for new patients from all sources totaled 107 during the 12.5 months of data collection. Referral for patients previously seen by other urology department providers totaled 22.

The six weeks after the clinic opened few men were scheduled \((n = 33)\) over three half-day clinics (Figure 3). At the end of 2015, despite the modest number of men meeting the inclusion criteria for the CUO study, overall new referrals remained steady, averaging 26 per fiscal quarter (Figure 4). In 2016, the clinic opened every Tuesday. As of the third quarter of 2016, referrals directly to this clinic continued to increase (after data collection closed) from both within UMHS and from other health systems, especially from local providers in the Ann Arbor area.

Designating a specialty clinic also clarified staffing decisions on these individual clinic days. There was little need for nursing care/teaching or for additional medical assistant involvement, both which incur additional staffing costs. The 45-minute new patient appointments permitted adequate time for the nurse practitioner (principle investigator) to review the potentially extensive medical records of this patient group and proceed with evaluation of the individual men.

The UMHS Department of Urology has over 38,000 visits yearly. Prior to the opening of this new clinic, 14 providers within the adult urology department accepted referrals for men with testicular or genital pain. During the study period of 12.5 months (June 16, 2015-June 30, 2016), a total of 228 men were scheduled into the newly established Chronic Male Genital Pain clinic (primary screening). Of these 228 patients, 107 were new referrals, 15 patients were scheduled for a second opinion (previously seen by other providers within urology) and 106 had been seen previously by the principle
investigator for pain issues and scheduled for a return visit prior to start of this study (Figure 3).

Of the 228 men who met primary screening (meaning scheduled into the Chronic Male Genital Pain clinic), 125 were deemed non-CUO at second level screening due to determination of pain or other presenting complaints at sites other than scrotal/testicular pain. The most predominant concern was erectile dysfunction without pain ($n = 41$), pain localized to the penis or early Peyronie’s disease (combined $n = 21$) and non-chronic genital pain ($n = 27$). Additional complaints that were not consistent with CUO are noted in format of a STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) diagram (Figure 5). An additional 83 of the 228 men were deemed non-CUO, due to identified etiologies, most predominantly bilateral varicoceles ($n=46$) and 74 additionally identified conditions (Figure 5). A listing of treatments and coded diagnosis are shown in Tables 5 and 6 respectively. A treatment algorithm summarizing the processes of evaluation in specialty feasibility clinic is shown in Figure 6.

Twenty men of the 228 men screened by the principle investigator met the study inclusion criteria for the CUO project (Chapter 4). Of these, all 20 consented and agreed to complete additional survey instruments. Survey instruments and additional contact with participants potentially could reveal additional reasons for their pain, but go beyond the scope of this first study focusing on establishing the clinic’s feasibility.

**Discussion**

Of the 38,000 patients seen in the UMHS Department of Urology, results of this feasibility study revealed that less than 1% of men presented with true chronic unexplained orchialgia, as established *a priori* by conceptual criteria. This feasibility
study evaluated viability of a method for identifying a source population of CUO for future study. It suggests the potential benefits of a dedicated subspecialty clinic for CUO within an academic urology practice, led by a nurse practitioner; most of these men could be treated according to a known underlying cause of their condition.

One of the most conspicuous outcomes was that far fewer men than originally anticipated had truly unexplained chronic orchialgia. Many men had an identified etiology for pain, and a source of pain that might respond to a surgical procedure. The number of men proceeding with surgery was not captured for this feasibility study, as conservative symptom management was the first course of treatment pursued during the timeframe of data collection. Despite the small sample of men with true CUO, 83 of the men who were thought to have CUO were provided with an accurate diagnosis. While this represents a positive clinical outcome, this did not support the initial hypothesis that ~30% of men would be identified with true CUO at time of initial clinic evaluation.

It is possible that a clinic designed to accommodate and fully evaluate patients for “unexplained” testicular pain may lead to referrals of non-surgical chronic pain patients, who required additional clinic time to more fully determine the underlying cause of their presenting complaint. The specialty clinic was designed for 45-minute appointments, which included adequate time for full record review. Furthermore, this finding of additional time for necessary evaluation, and creation of a clinic designed to provide that time supports a busy urological practice by allowing surgeons to focus on patients more likely to be surgical cases.

This expanded appointment time was vital and allowed for a more in-depth assessment of their symptoms and avoiding a missed explanation for chronic pain. Men
with chronic genital pain often present with record sets from multiple providers, or record sets that span many years. Men excluded from meeting CUO criteria had etiologies for their testicular pain that were readily identified with scrotal ultrasound (such as varicoceles or spermatoceles), a thorough history, and precise physical examination. Many men referred to the clinic with CUO presented without this imaging examination. This is particularly problematic in the case of ruling out high-risk entities such as cancer, as demonstrated by the single patient that was eventually diagnosed with a germ cell tumor as a result of his presentation to the Chronic Male Genital Pain Clinic.

Findings from this study highlight that there may be a lack of standardized evaluation of this population. Although an algorithm (Levine & Hoeh, 2015) for evaluation of chronic orchialgia does exist, it is based on expert clinical opinion and few providers in the community may not be aware of this algorithm to guide their evaluation. This may highlight a system issue in the dissemination of knowledge relative to a particular urology and pain subpopulation.

Increased awareness of this clinic among providers within the Department of Urology dispelled misconceptions that it required additional nursing and medical assistant support. This began a pattern of internal referrals for chronic male genital pain, for men who had been evaluated by other adult urology providers and promoted consistent scheduling. Since the beginning of the focused Chronic Male Genital Pain clinic in UMHS adult urology, men have been gratified to know that there is a focused clinic for their specific complaints, making referrals to this specialty clinic easily accepted by men meeting referral criteria (personal communication, J. Dupree, April 12, 2016).
Potential for Economic Implications

Oomen et al. (2014) suggested that in a given urology environment “a single urologist specializes in TPS [testicular pain syndrome; synonym for CUO] in order to prevent superfluous diagnostics that lead to delays in treatment” (p. 1725) and further advocates for a multidisciplinary approach to chronic testicular pain management. The benefit of an NP in a specialty role promotes continuity of care within any department, and avoids urgent care, retail clinic and emergency room use for specific complaints (in this case chronic male genital pain). This specialty NP clinic helps to “sort” patients according to providers with the appropriate expertise and appropriate interest in category of patients and ensures timely access to care.

Care provided by NPs and physicians has been repeatedly demonstrated equivalent for many chronic conditions (Horrocks, Anderson, & Salisbury, 2002; Stanik-Hutt et al., 2013; Newhouse et al., 2011; Poghosayn, Boyd & Knutson, 2014). However, it is not difficult to extrapolate the quality of care from comparison studies in primary care, as many urology conditions benefit from chronic, episodic long-term care, a role uniquely suited to the NP. A recent RAND study (Auerbach et al., 2012) reported that an NP in the primary care setting may be salaried 20-35% less than a physician. This implies that inclusion of NPs in the urology is a likely cost-effective way to increase access and patient management, especially for conditions that can be managed non-surgically. The burden of urologic diseases in the US continues to rise due to the aging population, encouraging movement of NPs into urology. This expansion of NPs into urology may eventually impact prices and utilization of urology services, although it is difficult to predict, as NPs cannot offer independent surgical services.
Urologic Diseases in America ([UDA], US Department of Health and Human Services, 2012) provides economic data for a variety of common conditions in urology. With the exceptions of erectile dysfunction and Peyronie’s disease surgeries, UDA does not report on male genital-specific surgeries. This creates an unknown in the surmised cost burden for surgical treatments of CUO. For example, there is no UDA data for surgeries that may successfully treat chronic testicular or scrotal pain (e.g., varicocelectomy, epidemectomy). The closest estimation is the cost for treatment of testicular cancer: 2006 charges across the US for ambulatory surgery (orchiectomy) totaled $23,609,028. Some men with CUO may undergo orchiectomy, like men with testicular cancer, but in (presumably) much smaller numbers. Table 7 shows cost averages at University of Michigan Health System for selected procedures that can be associated with treatment for men thought to have chronic unexplained orchialgia.

Future Implications

The results of this study emphasize the issue of who should see particular groups of patients, not solely who can. In a large academic center with many specialized clinics and providers, this new clinic offered innovative and streamlined care for men with CUO. Chronic unexplained orchialgia is not commonly a surgical or interventional diagnosis, likely making it less cost-effective for a trained surgeon to be the initial point of contact. Exploration of the clinic’s cost-effectiveness was beyond the scope of this initial feasibility study, but evaluation of cost comparison is a necessary component to consider in the future.

The Chronic Male Genital Pain clinic now exists as a subspecialty referral option for providers who evaluate men with chronic genital pain, but currently excludes men
with pelvic pain complaints. Its ongoing goals are (a) patient evaluation, (b) coordination of referrals to other services, (c) education of men (and partners when present) regarding their ongoing management and evaluation needs, (d) discussion of their role in developing a treatment plan, and (e) emphasis of the individual’s role in his own self-care as a chronic pain patient. This new clinic may also decrease an unknown patient cost burden by avoiding multiple clinic appointments for the same presentation. This project is also consistent with the IOM (2011) mandate to take advantage of currently available services to promote the management of patients with chronic pain.

**Limitations**

Study limitations include that the scheduling process was subject to considerable sampling group contamination, as the result of a lack of precision in scheduling. Men with other GU concerns were scheduled into this clinic, either to meet mandated new patient access requirements or due to open appointments. A single provider (who was also the principal investigator) completing physical examination may be another limitation, and may have introduced bias.

The strict inclusion criteria may have eliminated some men, such as those with chronic but episodic, rather than constant, pain that would have provided additional insight into chronic orchialgia. The inclusion/exclusion criteria prevented exploration of chronic orchialgia in the related population of men with chronic urologic pelvic pain syndrome (UCPPS) who often report chronic genital pain in addition to pelvic or perineal pain. Their inclusion may have expanded the numbers of men completing the instrument packet, adding additional strength to the study conclusions suggesting the characteristics of this chronic pain subpopulation. The costs of this clinic were not examined, although it
is anticipated that the clinic would have very low overhead in terms of supplies and staffing support.

**Conclusions and Clinical Implications**

In the absence of an evidence-based algorithm for treatment, men with CUO may pass back-and-forth among different providers and among different specialists. This feasibility study supported the initial aim to create a source population of men with CUO, although it was less than 30% anticipated. This research highlights the potential benefits of a subspecialty clinic that can fully accommodate the process for differential diagnosis for men presenting with complaints of chronic pain in the genital area. The clinic evaluation assured that the CUO label was appropriately applied only to the very few men without a meaningful known etiology, so that supportive care in living with these unknowns and symptoms can be offered.

Considering the latter, it may be particularly beneficial for the specialty CUO clinic to be staffed by a nurse practitioner with expertise in non-operative urology diagnosis and treatments. The innovation represented by this unique clinic is that it directs the scheduling of a nonsurgical urology pain population, and focuses it to an expert nurse practitioner. It has the benefit of removing predominantly non-operative patients from the schedules of surgeons, allowing them to focus their clinic time toward patients who may need surgical intervention.

This specialty clinic offers a more streamlined approach for men, in that they are scheduled with an expert provider who has the time, interest and skills to evaluate their specific concerns. The success of this feasibility project demonstrates the potential for a clinic designed to provide high-quality care to a specific population within urology,
building an infrastructure for research while also developing an evidence base that addresses specific knowledge gaps about men with chronic unexplained orchialgia.
References


Table 4

**Adult Male (> 18) Chronic Genital Pain Referral Guidelines**

| Suggested pre-referral evaluation and management guidelines | • Men with persistent genital pain (> 3 months)  
| • Emergent referral to Emergency Department if acute onset: see testicular pain guidelines  
| • If concern for testicular mass: see testicular mass guidelines  
| • This *excludes* patients with existing diagnoses, such as inguinal hernia, hydrocele, varicocele  
| • Symptomatic management:  
| • NSAIDs  
| • discretionary use of narcotics |

| Suggested additional testing and management prior to specialty clinic visit | Patients should have a scrotal ultrasound on record within the last 3 to 6 months, or have one scheduled in advance of the clinic visit |

| Specific patient education or information | None |

| Appointment timeframe | Next available |

Table 5

**Treatments Offered in the Chronic Male Genital Pain Clinic, Based on Suspected Etiology for Testicular Pain**

- Conservative, symptomatic management (e.g. use of compression shorts for support)
- Discussion of varicocele repair, hydrocele repair, epididymectomy, cyst removal
- Direction for management of constipation
- Treatment of prostatitis
- Referral for physical therapy (evaluation for posture, pelvic tilt, core strength abnormalities)
- Referral for pelvic floor physical therapy
- Trial of nonsteroidal anti-inflammatory drugs with or without muscle relaxers
- Trial of neuromodulator medication
- Referral to psychology or psychiatry for evaluation and management of stress-related issues or anxiety
- Conservative management attempted before spermatic cord block or referral to Anesthesia Pain Service for consideration of other nerve blocks
Table 6

*Diagnoses Coded for > 5 Visits in the Male Chronic Genital Pain Clinic*

<table>
<thead>
<tr>
<th>ICD-9 code</th>
<th>n</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>608.9</td>
<td>101</td>
<td>Testicular/scrotal pain</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Scrotal pain</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right or left testicular pain</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Orchialgia</td>
</tr>
<tr>
<td>456.4</td>
<td>46</td>
<td>Bilateral varicoceles</td>
</tr>
<tr>
<td>607.84</td>
<td>41</td>
<td>Erectile dysfunction</td>
</tr>
<tr>
<td>789.09</td>
<td>26</td>
<td>Bilateral groin pain</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right or left groin pain</td>
</tr>
<tr>
<td>257.2</td>
<td>20</td>
<td>Hypogonadism</td>
</tr>
<tr>
<td>608.98</td>
<td>18</td>
<td>Testicular cyst or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Epididymal cyst</td>
</tr>
<tr>
<td>608.86</td>
<td>18</td>
<td>Scrotal swelling</td>
</tr>
<tr>
<td>607.9</td>
<td>17</td>
<td>Pain in penis or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Penile pain</td>
</tr>
<tr>
<td>608.9</td>
<td>10</td>
<td>Epididymal congestion pain or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>post-vasectomy pain syndrome</td>
</tr>
<tr>
<td>278.01</td>
<td>10</td>
<td>Obesity</td>
</tr>
<tr>
<td>456.4</td>
<td>9</td>
<td>Unilateral varicocele</td>
</tr>
<tr>
<td>603.9</td>
<td>9</td>
<td>Hydrocele</td>
</tr>
<tr>
<td>608.1</td>
<td>6</td>
<td>Spermatocele</td>
</tr>
<tr>
<td>564.0</td>
<td>6</td>
<td>Constipation</td>
</tr>
</tbody>
</table>

* Diagnoses are not mutually exclusive; many men had multiple diagnoses.
Table 7

Cost of Selected Outpatient Procedures Performed in the Context of CUO

<table>
<thead>
<tr>
<th>Procedure</th>
<th>CPT Code</th>
<th>Average cost at UMHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spermatic cord block</td>
<td>64425</td>
<td>$2,427</td>
</tr>
<tr>
<td>Orchiectomy</td>
<td>54520</td>
<td></td>
</tr>
<tr>
<td>Orchiectomy, Radical</td>
<td>54530</td>
<td>$16,547</td>
</tr>
<tr>
<td>Epididymectomy, unilateral</td>
<td>54860</td>
<td>$11,504</td>
</tr>
<tr>
<td>Epididymectomy, bilateral</td>
<td>54861</td>
<td>$14,421</td>
</tr>
<tr>
<td>Microsurgical subinguinal varicocele repair, unilateral</td>
<td>55530 69990*</td>
<td>$19,760</td>
</tr>
<tr>
<td>Microsurgical subinguinal varicocele repair, bilateral</td>
<td>55535 69990*</td>
<td>$21,317</td>
</tr>
<tr>
<td>Microsurgical denervation of spermatic cord</td>
<td>55899 69990*</td>
<td>$19,000-$21,000</td>
</tr>
</tbody>
</table>

* Code for use of microscope during the procedure.

Figure 3. Utilization of Chronic Male Genital Pain Clinic June 15, 2015-June 30, 2016. NP: new patient to UMHS Urology; NP-2nd opinion: patient previously seen by UMHS urology provider; RV: return visit.
Figure 4. Pattern of New Patient Referrals to Chronic Male Genital Pain Clinic by Fiscal Quarters. (Note. Last two weeks of June 2015 included with July-Sept 2015 numbers).
Figure 5. STROBE Diagram for the Feasibility Testing Project.
Figure 6. Algorithm for evaluation in Chronic Male Genital Pain clinic.
Chapter 4

Descriptive Case Series of Men with Chronic Unexplained Orchialgia

Background

Patients with chronic pain often present with multiple symptoms that frequently have a poorly defined etiology, and there are wide variations within any group of patients having an anatomically-defined pain complaint. These variations highlight the need in clinical research to carefully delineate observable traits, characteristics, behaviors, and burden as necessary to guide effective treatment for this specific subgroups of patients by stratifying likely etiologic mechanisms. Ultimately, this should result in improved algorithms guiding treatment.

Chronic unexplained orchialgia (CUO) is one such chronic pain syndromes, and clear etiological explanation. As such, clear and complete identification of variance in observable traits, characteristics, behaviors, and economic and psychological burden of the CUO syndrome is lacking. Recognition of these aspects is needed to establish contributions from any particular dimension of the multifactorial symptoms reported with CUO. This level of clinical detail can lead to logical progression of individualized treatment strategies and reduce frustration for patients with a trial-and-error approach. Currently, definitions of CUO are based on expert opinion rather than empirical evidence.
and continue to undergo revision.

Chronic male genital pain is currently classified by alleged anatomic site of pain. However, the possibility exists that this is not an accurate representation of the actual cause or pathway for this particular chronic pain. Recognition and treatment of CUO, along with establishing criteria for its prevention and assessment, lags significantly behind most other non-malignant genitourinary diagnoses (e.g. incontinence, interstitial cystitis, male-factor infertility, benign prostatic hyperplasia) increasing the burden to men and the healthcare system.

Past investigations of CUO provide a sparse demographic representation of men with CUO and lack key details to aid understanding of this as a chronic condition. Past studies have not characterized specific pathophysiologies for CUO, reliable, effective therapies have not been identified, and exploration of men’s sexuality in a CUO context is lacking.

Prevalence of CUO is unknown. It is possible that much of what falls under complaints of chronic testicular pain or chronic male genital pain may not reach specialists such as urologists or pain management specialists. Taken together, this creates a void in standardizing a process for evaluation and management within known variance. Data are also lacking relative to prevalence, onset, natural history, and outcomes of CUO. One estimate of prevalence among clinical patients used the method of simply asking nurse practitioners to estimate how many men with CUO were seen in their individual clinics in an average 30-day period (Quallich, 2016). Nurse practitioners estimated a prevalence of 2.12%; the prevalence rose to 3.57% in the clinical sample of urology-focused nurse practitioners and dropped to 1.77% in the clinical sample for generalist
nurse practitioners (Quallich, 2016). But this best-guess estimate may not reflect an accurate prevalence, nor the larger sample of men with chronic genital pain who do not present to clinics.

Given the lack of additional contemporary estimates of prevalence and the paucity of studies fully describing men with CUO there is a desperate need for data on variance in traits, characteristics, behaviors, and burden on men and their families. Without this full descriptive data, comparisons with other chronic pain samples are limited.

The long-term goal of this line of inquiry is building the evidence base for demographic, medical, psychosocial/ psychological characteristics of men with CUO along with their self-reported pain scores. The short-term goal of this study is to begin the process through descriptive case series that can elicit variance in men’s descriptions about the experience of CUO.

The significance of the work is that by administering an extensive battery of instruments to men with CUO, clinically relevant parameters may be identified that suggest specific aspects for further investigation on a larger scale. This case series study may also suggest subset of instruments for eventual use in everyday practice to guide treatment decisions.

Aims and Hypotheses

These aims and hypotheses are designed to generate data that begins to address the gaps in knowledge and establish a knowledge base of men with CUO to guide future study and treatment.
Aim 1. To determine the feasibility of asking men with CUO to complete a lengthy survey battery of tools (some with sensitive information) to in a group of men with CUO.

Hypothesis 1: >80% of men diagnosed with true chronic unexplained orchialgia at time of clinic evaluation will fill out every survey instrument.

Aim 2. Obtain pilot data to inform a future study designed to fully characterize the biopsychosocial aspects of CUO.

Hypothesis 2: Men with chronic unexplained orchialgia will demonstrate comorbid symptoms associated with chronic pain.

Methods

Approval for data collection was granted by the Institutional Review Board of the University of Michigan (IRB-MED) eResearch ID: HUM00100294. Consent was obtained only after the clinic visit with the principle investigator had been concluded. The consent form emphasized that (a) choosing not to participate would not affect their care with Adult Urology at UMHS, and (b) the questionnaires would not be entered into their medical record.

Design

This pilot study used a cross-sectional design to explore the chronic pain experience of men with CUO, carefully diagnosed by having ruled out all known etiological underpinnings. For each CUO patient case identified, the man was asked to fill out an extensive, comprehensive battery of survey instruments (16 total). Instruments were chosen for their ability to measure the variety of domains represented by the Biopsychosocial Model (Engel, 1977) and the manner in which the blending of
biologic/physiologic, psychological, social and behavioral factors influence both one’s presentation and perception of pain. The study instruments were completed only once.

Sample

Twenty men with CUO were recruited from an academic urology department within a tertiary hospital system. Participants were approached to enroll in the study after completing a routine clinic visit with the urology nurse practitioner who confirmed they met study inclusion criteria.

Participants were men older than age 18 referred to adult urology outpatient clinic at a tertiary care hospital system in the Midwest. Inclusion criteria included:

- Agreement to complete the data collection survey instruments;
- Reported pain that localized to one or both testes;
- Reported response of at least “one” on pain, pressure or discomfort scales;
- The primary investigator determined that the source of their pain was the testes, and had ruled out potential causes of scrotal content pain (e.g. spermatocele, post-vasectomy pain, inguinal hernias) and had truly unexplained pain at the time of the clinic visit.

The exclusion criteria were modeled after the NIDDK’s Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) study, as men with chronic genital pain, and specifically chronic orchialgia, are excluded samples in this large multicenter study (Clemens et al., 2014; Landis et al., 2014). Men were excluded from participation in the present study if they had orchialgia but also a previous diagnosis of

- Interstitial cystitis (IC)/painful bladder syndrome (PBS)and/or chronic prostatitis (CP)/chronic pelvic pain syndrome (CPPS);
• An on-going neurological disease or disorder affecting the bladder or bowel;
• Cystitis caused by tuberculosis, radiation therapy or Cytoxan/cyclophosphamide therapy;
• Augmentation cystoplasty or cystectomy;
• Systemic autoimmune disorder (such as Crohn's disease or ulcerative colitis, lupus, rheumatoid arthritis, or multiple sclerosis);
• Cancer (with the exception of skin cancer);
• Major psychiatric disorder or other psychiatric or medical issues that would interfere with study participation (e.g. dementia, psychosis, upcoming major surgery, etc);
• Severe cardiac, pulmonary, renal, or hepatic disease that in the judgment of the study investigator would preclude participation in this study;
• Transurethral microwave thermotherapy (TUMT), transurethral needle ablation (TUNA), balloon dilation, prostate cryo-surgery, or laser procedure.

No adult men were excluded from this study based on their status as part of a minority group or subgroup, and no specific attempts at recruitment of minority groups was made. Sexual orientation or previous evaluation in a urology clinic or pain clinic did not exclude men from participating; although the clinic intake forms survey sexual orientation, the aim was to capture as diverse a sample as possible.

**Study Instruments**

As part of the Chronic Male Genital Pain clinic visit, a supplemental history and physical form was administered to capture additional information that contributes to the evaluation and management of chronic pain conditions. Extensive descriptive information
was collected, including family history (including family members with a chronic pain condition), complementary and alternative medicine use, previous medications and procedures, past and specialty providers that the subject may have visited, and any secondary pain sites.

Per the second aim of the study, extensive paper-based survey data was gathered. A primary consideration for this study is the fact that no psychometric tool has been established as reliable and valid in this particular chronic pain subsample. However, all of the instruments selected have been validated in various chronic pain samples and in gender-specific samples.

**Instrument choice.**

The instruments chosen represent a combination of legacy instruments and newer instruments that reflect the contemporary understanding of the field of chronic pain (Table 8). Specific psychometric instruments were chosen because of their frequent use for the evaluation of chronic pain samples and their previously established reliable psychometric qualities. These instruments evaluate the domains of pain, types of pain, associated comorbid conditions and allied symptoms, mood and functional status. The multiple instruments demonstrate conceptual clarity, making them valuable in establishing sample characteristics, with the potential long-term goal of selection amongst these tools for best use in generating data needed on observable traits, characteristics, behaviors for chronic orchialgia to guide clinical practice in the future.

The final set of instruments was chosen because most have been administered in pain samples, have validity data in male samples, and have proven stable factor structures. Additionally, this comprehensive set of instruments matches those used in the
Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) study. Choosing instruments that parallel many of those used in the MAPP study preserves the opportunity for eventual comparison of results from this project with those of the much larger MAPP effort, in which men with orchialgia were excluded. The 16 survey instruments chosen and organized by the Biopsychosocial Model is provided in Table 8, along with data on reliability. An alphabetized list of instruments with a brief summary description of each one is provided in Appendix C.

Many instruments were rejected for various reasons, and these instruments are listed in Table 9. Rejection of instruments was because they (a) were not validated with chronic pain patients, (b) overlapped with instruments that had been chosen, (c) or lacked strong psychometric properties.

The instruments as a whole are subject to recall bias, as is typical of most survey instruments. Each instrument selected was constructed at a 5th-6th grade reading level, considered to be relatively short tools to complete in and of themselves, and could be self-administered. Based on the literature, the selection of instruments could take up to 40-60 minutes to complete.

Data Management and Statistics

Visual inspection of the 16 instruments prior to data entry did not reveal any individual items that were routinely unanswered. Data was entered into IBM SPSS® version 24 (IBM Corp., US). Raw data for the PROMIS instruments was uploaded to help@assessmentcenter.net, and transformed T scores were returned to the investigator via email. Raw data for the SF-12 instrument was similarly uploaded to OptumInsight Life Sciences, Inc., and after scores were transformed and a summary of the results was
made available through the OptumInsight web platform. Other study instruments were
totaled or transformed as necessary. Results were subjected to normality checks via
graphic display and using Shapiro-Wilks tests, as the sample size was small. The data
were checked for outliers using boxplots or bar graphs. Initial analysis of the
demographic data was completed with exploratory descriptive methods to evaluate for
patterns by age groupings, medications or number of previous procedures.

**Results**

Of the 20 men who met the inclusion criteria, all 20 agreed to be consented to
complete the study and survey instruments. Twenty men were provided with the full
packet of 16 survey instruments and a supplemental history form exploring medication
use and additional demographic information. Return rate for the completed survey battery
was 70% (14 of 20). Of the 14 survey packets returned, 12 were completed in full, with
only few individual items across the multiple instruments unanswered. The remaining 6
packets were not returned. Review of the instruments prior to data entry did not reveal
any instruments that were routinely left blank or any individual items that were routinely
unanswered. Few instruments had outliers, and these men were randomly distributed
across the survey instruments. Table 10 presents results from all the survey instruments
as median and range, as well as the dimension of chronic pain measured.

**Social Perspective Results.**

The median age in the study sample was 48.5 years (range 24-64). Additional
demographics are shown in Table 11. No patients reported receiving disability payments
and none were involved in pending legal action. Only one man had made use of
complementary and alternative medicine treatment (acupuncture) and previous specialist
evaluation was limited to another urology provider (n = 5) or a pain specialist for back pain (n = 2). No participant reported an active opioid contract with any provider.

Results on the SF-12 (Figure 7) revealed that 57% of the sample are at risk for screening positive for depression when compared with the general sample. Men demonstrated some limitations in self-care, physical, social, and role activities, as a result of bodily pain and fatigue. The participants demonstrated lower than instrument norm scores for self-care, walking, and involvement in physical activities on SF-12 scoring. Limitations were noted to typical role activities due to overall physical health, but men demonstrated sample norm values for general health. Social functioning and emotional role were limited, and participants demonstrated some overall compromise to emotional cognitive and intellectual function, as measured by the SF-12.

Results on the SEAR (Table 10) demonstrate only mild-moderate issues with relationship satisfaction and high self-esteem and confidence in their sexual ability.

**Biology-based Perspective Results.**

Clinical information from the CUO sample is presented in Table 12; all results are median scores, due to the small sample size. The median duration of pain was 38.69 months (range 3-72 months). 72 months represented an outlier that reported pain duration that was 28 months longer than the next longest time. A median of 76% of the overall pain complaint was associated with a primary site of pain, although two of the 14 men reported only 15-20% of their pain was from the testes. Table 13 shows information about oral medication use.

Results from the American College of Rheumatology criteria measuring widespread and centrally-mediated pain (Wolfe et al., 2010) suggest this small sample
did not meet diagnostic criteria for a widespread pain syndrome (median score = 1.00). The sample demonstrated minimal-moderate interference from pain, based on median scores that were below threshold for diagnosis. Men did report some areas of pain in the last week that included left upper arm ($n = 2$) left lower leg ($n = 2$) abdomen ($n = 1$) lower back ($n = 2$) or neck ($n = 1$).

Median American Urological Association Symptom Index (AUASI) scores (measuring lower urinary tract symptoms in men) demonstrated a low incidence of urinary symptoms (6.00); this total score indicates minimal urinary bother (Table 10). Median results on the Male Genitourinary Pain Index (M-GUPI) were midrange for the total instrument (19.00), and demonstrated low urinary symptoms (1.00) on the urinary subscale. Participants reported midrange median scores for the pain subscale (10.00) and moderate impact to quality of life on the QOL subscale (8.00).

**Biology/Psychology-based Perspective Results.**

Scores on the Brief Pain Inventory (BPI) (Table 10) demonstrated both moderate pain severity (19.00) and mild-moderate interference from pain, with a median pain score of 4.00. Results from the body map demonstrated both left ($n = 8$) and right groin ($n = 3$) were areas of increased pain in this sample, and that the scrotum ($n = 11$) was the primary site of most genital pain ($n = 10$), as the BPI body map does not specify testes.

The total score (55.00) on the International Index of Erectile Function (IIEF) (Table 10) showed some moderate erectile dysfunction in the sample (Table 9). The orgasmic (10.00) and desire subscales (8.00) showed low dysfunction, and the overall satisfaction score (6.00) and intercourse satisfaction score (9.00) showed moderate to
high satisfaction. The erectile dysfunction subscale showed mild to moderate dysfunction (20.50).

To further explore the data, a comparison between the median pain, worst pain, and current pain item individual item scores on the BPI and PainDETECT instruments is shown in Table 14. This comparison tested consistency in pain reporting in the study sample, as both measure the same concept and are measured on 10-point Likert scales. Median results for all three domains are similar.

**Psychology-based Perspective Results.**

Participants reported median midrange scores for all domains on the Beliefs in Pain Control Questionnaire (BPCQ), indicating indeterminate beliefs in the three concepts measured on this instrument (Table 10). Participants did not demonstrate clear evidence for internal locus of control (15.00), belief in chance happenings (11.00) or that “powerful doctors” control the course of their pain treatment (13.50). Median results on the Coping Strategies Questionnaire (CSQ) subscale demonstrated participants believe in a low control over their own pain (2.00) and evidence for little belief in their own ability to decrease their pain (2.00). Participants showed low median scores for the overall instrument (5.00), indicating minimal evidence for catastrophizing in the study sample, although one participant scored very high (35.00).

Participants demonstrated little evidence for depressed mood, as scored on the Hospital Anxiety and Depression Scale (HADS). This instrument (Table 10) showed a normal depression score (median 4.00) and a slightly higher median anxiety score (8.00). The CUO sample scored a median for fatigue of 58.35 on the Patient-Reported Outcomes Measurement Information System (PROMIS) Fatigue instrument, and a PROMIS sleep
disturbance median score of 54.8. Both PROMIS instruments demonstrated a gradual increase across the reported range of scores, without outliers.

Patients reported self-identified an overall moderate decrease in their cognitive ability (Table 10) on the Multiple Ability Self-report Questionnaire (MASQ), most notable in the attention and concentration subscale (35.00) and language subscale (28.00). Other domain scores were midrange, indicating indeterminate decline to cognitive ability.

Scores on the PainDETECT did not suggest a neuropathic cause for chronic orchialgia in this group. The median score on this instrument was 4.00, and overall median score was 12.38 (range 5-38); the 38 represented an outlier (Table 9).

Results on the Positive and Negative Affect Schedule (PANAS) demonstrated more positive affect (median 34.00) in this group than negative affect (median 19.50).

Results on both the instruments that evaluate trauma, the Childhood Traumatic Events Scale and Recent Traumatic Events Scale (CTES/RTES) instruments, demonstrated that death of a friend or family member was the most frequently reported source of trauma in this group, both as adults (n = 5) and as children (n = 6). Parental upheaval appeared as a factor for childhood trauma (n = 5). Four men reported a change in work in the previous 3 years. No participants reported a history of a traumatic sexual experience either as a child or an adult.

**Discussion**

This is the first project of its kind to extensively evaluate men with precisely defined chronic unexplained orchialgia using standardized psychometric tools. As a cross sectional study, it serves as the foundation for future studies seeking to evaluate this specific sample of men. Use of standardized psychometric tools promotes the comparison
of chronic unexplained orchialgia with other chronic pain samples, and begins to establish study feasibility and estimates of response ranges in men with CUO.

This pilot sample demonstrated willingness to complete the extensive battery of tests, despite the extensive number of individual instruments. This offered an exploration of the multidimensional aspects of their pain experience, offering preliminary evidence for this study design as a feasible method for future date collection with this phenomenon. The personal nature of CUO made it uncertain that men would be open to questions about genital health, general pain or comorbid pain symptoms, despite their presentation in clinic seeking care. Hesitation to reveal details that did not seem directly related to their pain complaint may account for the six men who did not return the survey packets.

**Biopsychosocial Model Perspective on Results**

In terms of a social perspective, demographic results were similar to previously published results, with the exception of higher reported education and income than previously suggested by the literature (Davis et al., 1990; Costabile et al., 1991). Results from the SF-12 (Figure 7) vary greatly from all other 15 study instruments in this pilot study, showing much greater decline in function across all its domains, and increased depression risk. If the SF-12 were the sole screening tool used, the CUO sample would seem much more functionally affected by chronic pain than summary scores from the other instruments used in this pilot study.

**Biologic perspective.**

The lack of urinary symptoms in this sample was consistent with the previously published literature review (Quallich, & Arslanian-Engoren, 2013). Participants reported
meager use of pain medications (Table 13) despite a lengthy list of medications that may have been prescribed or recommended. In the CUO sample, there was no suggestion for a specific pain mechanism (e.g., centrally mediated pain) based on the American College Rheumatology criteria or PainDETECT results. Previous authors (Parekattil et al., 2013) offered evidence for a neuropathic component to chronic testicular pain.

A single participant \( (n = 1) \) scored very high on the PainDETECT, reported high interference on Brief Pain Inventory (BPI) pain interference subscale (9.57) and showed evidence for widespread pain based on the ACR criteria. This suggests that future investigations into CUO samples may uncover evidence for a subtype of chronic orchialgia that is more similar in presentation to other widespread pain conditions.

**Combined biologic and psychologic perspective.**

Evaluation from a combined biology and psychology perspective revealed that the sites of genital pain were consistent between two measures in this study (Male Genitourinary Pain Index [MGUPI] and Brief Pain Inventory [BPI]). However, the BPI did not specify testes as a site for pain. Men did identify right-sided testicular pain (50%) which is consistent with previous reports in the literature (Quallich, & Arslanian-Engoren, 2013).

Results on the International Index of Erectile Function showed mild to moderate erectile dysfunction, lower orgasmic dysfunction and mild decrease to desire. This may be secondary to organic comorbidities, as well as demonstrating a contribution from chronic testicular pain. Self-esteem and Relationship Questionnaire scores showed a relatively high level of self-esteem and confidence in both relationships and sexual
function. This perspective has not been addressed in the literature, with the exception of a single study (Ciftci et al., 2011).

**Psychology perspective.**

Many of the psychological traits and allied comorbid symptoms reported with chronic pain were not evident in this sample. The sample showed low depression and anxiety scores, but no catastrophizing and low negative mood. This may be a function of the shorter duration of pain than previously reported in the review of the literature (Quallich & Arslanian-Engoren, 2013). The CUO sample median scored below the US sample mean for fatigue (58.35) but closer to the sample norm for sleep disturbance (median 54.8); the PROMIS fatigue results showed the most consistency with a chronic pain sample. Low catastrophizing in this group is consistent with their low median pain scores and suggests higher potential treatment success (Sullivan, 2009). Lower anxiety suggests the opportunity for increased treatment success.

Little is known about specific coping styles of men who have chronic pain (Keogh, 2015). The results of the Beliefs in Pain Control Questionnaire were inconclusive as far as highlighting a particular coping style in the limited CUO study sample.

Men in this sample showed moderate perceived deficit in language, attention/concentration on the Multiple Ability Self-report Questionnaire subscales. The median scores in the CUO sample were worse than those reported for fibromyalgia patients (the exemplar group for centrally-mediated pain) for the MASQ language and attention/concentration subscales (Williams, Clauw & Glass, 2011).
It is interesting to note that none of the participants in this study reported a history of traumatic sexual experience either as a child or within the last three years as an adult. This is in stark contrast to previous opinion in the literature, beginning with Schover in 1990. This is the first and only contemporary study to investigate this dimension of social history and potential comorbidity for chronic pain. Although this is a small sample size, sexual trauma was not noted in this pilot study. Further investigation in a larger sample size is warranted, as a history of sexual trauma has been demonstrated to be a contributor to chronic pain for women.

**Comparison with Other Studies.**

Despite the limitations of a small sample size, this sample offers the opportunity to compare the present results with the sparse published studies that have investigated the chronic genital pain in specific male samples.

Table 15 presents a comparison between IIEF scores in the present CUO sample and the sample from Ciftci et al. (2011). To date, these authors are the only paper to use of a standardized psychometric instrument, other than a visual analog pain scale, to measure other dimensions of chronic pain in men who have chronic testicular pain. They included 50 men using a broad inclusion criterion: “symptoms suggesting orchialgia” (Ciftci et al. 2011, p. 632). The CUO sample shows higher scores (better function) for the subscales, with the exception of the intercourse satisfaction and erectile function subscales. The similarities in the results between these two samples suggests that overall sexual function is affected by chronic orchialgia, either purely due to the site of discomfort with activity, the psychosocial burden of chronic pain or a different mechanism yet to be established.
Comparison across several instruments between the present CUO sample and early results from the male participants in the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) study is presented in Table 16. The samples share few similarities beyond age. The CUO sample reports a shorter duration of pain, a lower overall pain score, and an American Urological Association Symptom Index and Male Genitourinary Pain Index (MGUPI) scores total indicating little interference from urinary symptoms. The median scores for the MGUPI and its subscales demonstrate worse symptoms in the MAPP study group. Rates of anxiety are similar between the two groups and depression is slightly lower in the CUO sample. The MAPP group reported a much higher rate of erectile dysfunction as measured by the IIEF-6 (a shorter version of the International Index of Erectile Function).

Clemens et al. (2015) reported that perineal pain appears to be a defining characteristic in male UCPPS. The CUO sample did not choose this as a site of pain either on Brief Pain Inventory or MGUPI. The contrast between these two groups calls into question the rationale for categorizing chronic orchialgia as a subset of male pelvic pain, although men with UCPPS do report testicular pain. When using the presence of urinary symptoms and urinary pain or bother as defining characteristic of the UCPPS group, the chronic orchialgia sample did not share those same characteristics. Chronic orchialgia may be a distinct clinical entity; the choice to mirror the MAPP instruments and exclusion criteria for this CUO study creates a “control” sample that can be compared with the results of the MAPP analysis. Including men with UCPPS in future explorations of chronic orchialgia will offer a larger sample sample, and will contribute to a richer, more accurate phenotype.
Limitations

Consistent with the design of the study, this project offers an intense look at small sample of 14 men. Interpretation of the results are limited by (a) the small sample size; (b) lack of geographic diversity; (c) lack of racial/ethnic diversity; (d) a convenience sample from a single institution. These factors may inadvertently skew the results in terms of ethnicity and age, although this may be ameliorated by the fact that this academic setting serves as a tertiary referral center with a considerable watershed area from which referrals are generated.

Statistical analysis of the instruments is also limited due to the small sample size and the variable number of men who completed each instrument. Not all instruments were completed by all participants, limiting the total number of responses for evaluation on some instruments. One explanation for lack of return of the surveys may be that the packet was quite extensive, requiring approximately 40 minutes to complete. Completion of the full instrument packet varied by individual, and may have been influenced by the position of the individual instrument in the packet order.

Conclusion and Clinical Implications

The cross-sectional sample is described in more detail than has been previously presented in the only recent integrative review of the literature (Quallich, & Arslanian-Engoren, 2013). With the exception of visual analogue scales, previous studies have not included standardized assessment instruments, citing the rationale that there are no instruments specific to the CUO sample (Benson & Levine, 2012). The larger implication is that by reporting sparse demographic data and the choice not to use psychometric instruments in previous interventional studies, this may have contributed to
men being treated with interventional procedures and surgery unnecessarily, potentially a cost both to them and healthcare as a whole.

Performance on these instruments may also be in conflict with the actual clinical presentation. The report of pain as a chief complaint may be exaggerated, when compared with the rating on these instruments. The value of a thorough exploration of presentation with acknowledgment of the Biopsychosocial Model and the role of cognition in interpreting in maintaining chronic pain cannot be emphasized enough. Further study may suggest a causal or predictive model in this chronic pain subgroup that can be used to guide current treatment as well as future research.

This collection of multidimensional self-report measures will be used to improve understanding of CUO presentation as a way to estimate sampling need for future grant applications and the long-term goal of creating a clinical phenotype. A description of observable traits and characteristics may provide a better understanding of potential etiologies for CUO and may suggest specific targets for treatment. This multidimensional assessment of men with CUO will offer insight regarding the natural history, and provide guidance for measuring responses to treatment. Establishing psychosocial and comorbid allied symptoms, in particular, can suggest a subsample of men with CUO that may benefit from care in specialties outside of urology. This study moves the state of the science towards a multidimensional understanding of men with CUO that can be used to guide treatment decisions.
References


<table>
<thead>
<tr>
<th>Comparison Items</th>
<th>Concept measured</th>
<th>Time to complete</th>
<th>Measurement scale?</th>
<th>Subscale of larger instrument?</th>
<th>Factor structure</th>
<th>Reliability (Cronbach’s alpha)</th>
<th>Limitations</th>
<th>Additional comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>American College of Rheumatology criteria1</td>
<td>Fibromyalgia (centrally mediated pain)</td>
<td>Variable</td>
<td>Variable between questions</td>
<td>No</td>
<td>Two domains: widespreadedness of pain, symptom severity</td>
<td>n/a</td>
<td>Data is collected over the past week</td>
<td>“Body map” may allow for identification of other or secondary site pain that may aid in diagnosis of a more widespread neuropathic pain syndrome</td>
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<td>25 total items; Not all will be applicable to each patient</td>
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<td>Body map may be confusing for some patients</td>
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<tr>
<td>American Urological Association Symptom Index (AUASI)1</td>
<td>Severity of urinary symptoms due to BPH</td>
<td>2 to 3 minutes</td>
<td>0 to 5, zero representing “not at all”, five representing “almost always”</td>
<td>No</td>
<td>Two factors: Obstructive symptoms (4 questions) Irritative symptoms (3 questions)</td>
<td>Overall .85 Obstructive symptoms .82 Irritative symptoms .72</td>
<td>Data is collected over the past 4 weeks; may not sufficiently capture the pattern of chronic condition</td>
<td>Designed to be responsive to outcomes in BPH treatment</td>
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<td>7 items</td>
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<tr>
<td>Male Genitourinary Pain Index (M-GUPI)1</td>
<td>Genitourinary pain</td>
<td>2 to 3 minutes</td>
<td>0 to 5, zero representing “not at all”, five representing “almost always” but scale options vary based on question</td>
<td>No</td>
<td>Three factors: pain, urinary symptoms, quality of life</td>
<td>Pain .80 Urinary symptoms .73 Quality of life .74</td>
<td>Diagnostic criteria reflect practice criteria, and not clinical trial click criteria, which would be more specific</td>
<td>Represents a modification of the NIH-CPSI Single instrument that could be used to assess symptom severity with GU pain complaints</td>
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<td>10 items</td>
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<td>Comparison Items</td>
<td>Concept measured</td>
<td>Time to complete</td>
<td>Measurement scale?</td>
<td>Subscale of larger instrument?</td>
<td>Factor structure</td>
<td>Reliability (Cronbach's alpha)</td>
<td>Limitations</td>
<td>Additional comments</td>
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<tr>
<td>Brief Pain Inventory (BPI) Body pain map/ genital pain map</td>
<td>Pain</td>
<td>~ 5 minutes</td>
<td>0 to 10 point Likert scale</td>
<td>Yes</td>
<td>Two factors: Pain intensity (sensory dimension)- 4 items Pain interference (reactive dimension)- 7 items</td>
<td>Original study with cancer patients: .80-.87 intensity .89-.92 interference</td>
<td>Assumes that sensory and reactive dimensions of pain are stable over time</td>
<td>Assumes that activity interference is stable over time</td>
</tr>
<tr>
<td>International Index of Erectile Function (IIEF)</td>
<td>Erectile dysfunction</td>
<td>3-5 minutes</td>
<td>Likert type Range from “almost never/never” to “almost always/ always”</td>
<td>No</td>
<td>Five domains of sexual function: Erectile function Orgasmic function Sexual desire Intercourse satisfaction Overall satisfaction</td>
<td>Overall .93 Erectile function .94 Orgasmic function .94 Sexual desire .83 Intercourse satisfaction .83 Overall satisfaction .82</td>
<td>Only measures sexual function</td>
<td>Designed to be responsive to outcomes</td>
</tr>
<tr>
<td>Beliefs in Pain Control (BPCQ)</td>
<td>Beliefs about controlling pain</td>
<td>5 to 10 min.</td>
<td>6-point Likert type scale, ranging from “strongly disagree” to “strongly agree”</td>
<td>No</td>
<td>Three factors: Powerful doctors Chance happenings Internal scale</td>
<td>Overall .68 Powerful doctors .82 Chance happenings .56 Internal scale .74</td>
<td>Cautioned against use in pain-free samples</td>
<td>Internal consistency best with chronic pain patients</td>
</tr>
<tr>
<td>Items</td>
<td>Concept measured</td>
<td>Time to complete</td>
<td>Measurement scale?</td>
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<tr>
<td>Six-item Catastrophizing Subscale from Coping Strategies Questionnaire (CSQ) 2</td>
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<td></td>
<td>Evaluates a single point in time</td>
<td>Certain coping strategies may be associated increased distress and dysfunction</td>
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<td>PainDETECT 2 Pain</td>
<td></td>
<td></td>
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<td></td>
<td>Middle scores imply physical exam is necessary</td>
<td>Developed after exhaustive review of the literature to determine factors relative to patient experience of neuropathic pain syndromes</td>
</tr>
<tr>
<td>Childhood traumatic events scale/Recent traumatic events scale (CTES/RTES) 2</td>
<td></td>
<td></td>
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<td></td>
<td>Subject to reporting bias and recall bias</td>
<td>Constructed based on review of childhood abuse literature</td>
</tr>
<tr>
<td>Hospital Anxiety and Depression Scale (HADS) 2</td>
<td>Anxiety</td>
<td></td>
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<td></td>
<td>Present state of mood measured subject to how the patient is instructed to fill it out</td>
<td>Designed specifically for clinic/ outpatient use</td>
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<tr>
<td></td>
<td>Depression</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Designed to screen for &quot;clinically significant&quot; anxiety and depression (Zigmond &amp; Snaith 1983, page 364)</td>
</tr>
<tr>
<td>Multiple Ability Self-report Questionnaire (MASQ)</td>
<td>Self-appraisal of ability to perform basic cognitive functions</td>
<td>~ 5 minutes</td>
<td>Five-point scale “never” to “always”</td>
<td>No</td>
<td>Five domains: Language: 8 questions Visual perceptual: 6 questions Verbal memory: 8 questions Visual memory: 8 questions Attention/concentration: 8 questions</td>
<td>.92 for entire scale (Seidenberg 1994) language .74 visual perceptual .72 verbal memory .72 visual memory .73 attention/concentration .74</td>
<td>Not an objective measure of cognitive function Subject to recall bias Subject to subjective nature of judging one's own ability</td>
<td>Perceived decline in cognitive function is not the same as an actual decline in cognitive function Does not measure the effort required for particular cognitive function within the five measured</td>
</tr>
<tr>
<td>Positive and Negative Affect Schedule (PANAS)</td>
<td>Positive affect, or the extent to which a person feels enthusiastic active and alert Negative affect or subjective distress</td>
<td>5 to 10 minutes</td>
<td>5-point Likert type scale, ranging from “very slightly” to “extremely”</td>
<td>No</td>
<td>Two factors: Positive affect Negative affect</td>
<td>Positive affect .88 Negative affect .87</td>
<td>Sensitive to the specific instructions given with administration of the instrument May not possess factorial invariance across gender</td>
<td>Scales show low intercorrelations, suggesting the relative independence of the two subscales When used with short-term instructions, instrument is sensitive to fluctuations in mood Negative affect scale is related to perceived stress</td>
</tr>
<tr>
<td>PROMIS fatigue</td>
<td>Fatigue</td>
<td>1 to 2 min.</td>
<td>Five option Likert scale</td>
<td>Yes: larger question bank of 95 items</td>
<td>Two domains: Experience Impact</td>
<td>.91 for the short form</td>
<td>No longitudinal studies Unclear responsiveness to change 7-day recall self-reported</td>
<td>Individual questions have been pulled from legacy instruments Seven-day recall may not capture the full impact of the chronic condition Not disease specific; a general instrument</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th><strong>Comparison Items</strong></th>
<th><strong>Concept measured</strong></th>
<th><strong>Time to complete</strong></th>
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<tr>
<td>Instrument</td>
<td>Function</td>
<td>Time</td>
<td>Scale Type</td>
<td>Yes/No</td>
<td>Reliability</td>
<td>Longitudinal Studies</td>
<td>Responsiveness</td>
<td>Recalls</td>
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<tr>
<td><strong>PROMIS sleep</strong></td>
<td>Sleep</td>
<td>1 to 2 min.</td>
<td>Five option Likert scale</td>
<td>Yes: larger question bank of 27 items</td>
<td>.88 for the short form</td>
<td>No longitudinal studies</td>
<td>Unclear responsiveness to change</td>
<td>7-day recall self-reported</td>
</tr>
<tr>
<td><strong>Self-esteem and Relationship Questionnaire (SEAR)</strong></td>
<td>Erectile dysfunction</td>
<td>3-5 minutes</td>
<td>Likert type</td>
<td>No</td>
<td>Two factors: Sexual relationship, Confidence (self-esteem, overall relationship)</td>
<td>Unknown sensitivity in chronic conditions</td>
<td>Designed to measures psychological issues with erectile dysfunction</td>
<td></td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>Range from almost never/never to almost always/always</td>
<td></td>
<td></td>
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<tr>
<td><strong>Short Form 12 (SF-12)</strong></td>
<td>Functional health and well-being</td>
<td>1 to 3 minutes</td>
<td>Variable between questions</td>
<td>Yes: SF-36</td>
<td>Eight domains: Physical functioning, Role – physical, Role – emotional, Mental health: 2 questions Bodily pain, General health, Vitality, Social functioning: 1 question each</td>
<td>.89 (Ware 1996)</td>
<td>Recall bias</td>
<td>Less precision than the full form SF 36</td>
</tr>
</tbody>
</table>

*All instruments have been validated in chronic pain and male populations.

*Note. Superscripts denote Biopsychosocial Model dimension. 1: Biology. 2: Psychology. 3: Social.*
<table>
<thead>
<tr>
<th>Instrument</th>
<th>Rationale for rejection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arizona Sexual Experience scale- ASEX 5 questions</td>
<td>Not specific to men; one of five questions changes based on gender but accurately measures presence of sexual dysfunction. Validated for use with depressed individuals; was specifically developed to evaluate psychotropic drug-induced sexual dysfunction and changes in sexual dysfunction.</td>
</tr>
<tr>
<td>Beck Depression Inventory- BDI 21 items</td>
<td>Developed to measure intensity of depression in patients with psychiatric diagnoses. Also used to diagnose depression in normal samples. Overlap with other instruments; goal of the project is not specifically evaluating depression in this sample.</td>
</tr>
<tr>
<td>Brief Sexual Function Questionnaire- BFSQ 33 total questions</td>
<td>Official description is 21 questions (some have multiple sections). Originally validated in depressed men; not widely used. Confusing scoring protocol focuses on specific sexual difficulties in the clinical context of depression, and erectile dysfunction generally.</td>
</tr>
<tr>
<td>Complex Multi-symptom Inventory (CMSI) 39 items</td>
<td>Identifies somatic conditions that usually accompany fibromyalgia. Aid in identification of high symptom burden and provides insight into decreased quality of life, decreased compliance with treatment, increase healthcare resource utilization, increase total healthcare cost. Overlap with other instruments.</td>
</tr>
<tr>
<td>McGill Pain Questionnaire- MPQ 20 item groupings</td>
<td>Static measure of pain without temporal considerations. Forces individual to select words that may not accurately describe pain.</td>
</tr>
<tr>
<td>Men’s Sexual Health Questionnaire- MSHQ 25 items</td>
<td>Validated only in men &gt;65. IIEF more widely used and recognized, allowing for better comparison with published data.</td>
</tr>
<tr>
<td>Neuropathic Pain Symptom Inventory- NPSI 12 items</td>
<td>Sparse literature only suggests neuropathic origin for chronic unexplained orchialgia, this has not been concretely established. Overlap with ACR criteria and PainDETECT.</td>
</tr>
<tr>
<td>Pain Anxiety Symptom Scale- PASS 40 items</td>
<td>Self-report instrument with four subscales. Unclear assessment of pain-related fear or anxiety; overlap in assessment of catastrophic thinking with CQS subscale.</td>
</tr>
<tr>
<td>SCL-90R somatization subscale 11 items</td>
<td>Measures if individual is somatising, but not symptoms indicative of somatic syndrome. More important to measure symptoms as insight into men that may be more difficult to treat; may have multiple pain sites and not only GU sites.</td>
</tr>
<tr>
<td>SF-36 36 questions</td>
<td>Although widely used, it has a lack of specificity for assessing established pain constructs.</td>
</tr>
<tr>
<td>Sickness Impact Profile- SIP 136 items</td>
<td>Long form. Impact of illness on daily function; overlaps with dimensions of other shorter instruments.</td>
</tr>
<tr>
<td>Survey of Pain Attitudes- SOPA 57 items</td>
<td>Dimensions measured by this instrument (medical care, pain control, solicitude, disability, medication) are captured by other instruments. In many studies, beliefs and coping are not clearly distinguish or defined, creating conceptual confusion and a lack of clarity regarding what this instrument actually measures.</td>
</tr>
</tbody>
</table>
Table 10

Results by Instrument and Pain Measurement Dimension

<table>
<thead>
<tr>
<th>Dimension of Biopsychosocial Model</th>
<th>Pain Measurement Dimension</th>
<th>Instrument (if present)</th>
<th>Subscale</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Scoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biology</td>
<td>Pain mechanism</td>
<td>American College of Rheumatology criteria Widespread Pain Index (WPI)</td>
<td></td>
<td>1.00</td>
<td>0.00</td>
<td>18.00</td>
<td>Range 0-19</td>
</tr>
<tr>
<td>Biology</td>
<td>Genitourinary symptoms</td>
<td>American Urological Association Symptom Index (AUASI)</td>
<td>Total score</td>
<td>6.00</td>
<td>1.00</td>
<td>25.00</td>
<td>Higher score = worse symptoms</td>
</tr>
<tr>
<td>Biology</td>
<td>Genitourinary symptoms</td>
<td>Male Genitourinary Pain Index (M-GUPI)</td>
<td>Total score</td>
<td>19.00</td>
<td>10.00</td>
<td>35.00</td>
<td>Total instrument range 0-45; Pain subscale range 0-23; Urinary subscale range 0-10; Quality of life (QOL) subscale range 0-12.</td>
</tr>
<tr>
<td>Biology</td>
<td>Genitourinary symptoms</td>
<td>Male Genitourinary Pain Index (M-GUPI)</td>
<td>Total score: Pain subscale</td>
<td>10.00</td>
<td>6.00</td>
<td>18.00</td>
<td></td>
</tr>
<tr>
<td>Biology</td>
<td>Genitourinary symptoms</td>
<td>Male Genitourinary Pain Index (M-GUPI)</td>
<td>Total score: Urinary subscale</td>
<td>1.00</td>
<td>0.00</td>
<td>6.00</td>
<td></td>
</tr>
<tr>
<td>Biology</td>
<td>Genitourinary symptoms</td>
<td>Male Genitourinary Pain Index (M-GUPI)</td>
<td>Total score: QOL subscale</td>
<td>8.00</td>
<td>3.00</td>
<td>12.00</td>
<td></td>
</tr>
<tr>
<td>Biology</td>
<td>Pain mechanism, intensity</td>
<td>Brief Pain Inventory (BPI)</td>
<td>Total score</td>
<td>32.00</td>
<td>13.00</td>
<td>82.00</td>
<td>Higher score = worse symptoms.</td>
</tr>
<tr>
<td>Biology</td>
<td>Pain mechanism, intensity</td>
<td>Brief Pain Inventory (BPI)</td>
<td>Relief score*</td>
<td>2.00</td>
<td>0.00</td>
<td>9.00</td>
<td>*This is a percent on the instrument, range 0-100</td>
</tr>
<tr>
<td>Biology</td>
<td>Pain mechanism, intensity</td>
<td>Brief Pain Inventory (BPI)</td>
<td>Pain severity subscale</td>
<td>19.00</td>
<td>6.00</td>
<td>31.00</td>
<td></td>
</tr>
<tr>
<td>Biology</td>
<td>Pain mechanism, intensity</td>
<td>Brief Pain Inventory (BPI)</td>
<td>Pain interference subscale</td>
<td>23.00</td>
<td>3.00</td>
<td>65.00</td>
<td>Total score range 0-110; pain severity score range 0-40; pain interference score range 0-70.</td>
</tr>
<tr>
<td>Psychology Biology</td>
<td>Male Sexuality QOL/functional status</td>
<td>International Index of Erectile Function (IIEF) ( n = 11 )</td>
<td>Total score</td>
<td>Erectile function subscale (IIEF-6)</td>
<td>Orgasmic function subscale</td>
<td>Sexual desire subscale</td>
<td>Intercourse satisfaction subscale</td>
</tr>
<tr>
<td>-------------------</td>
<td>--------------------------------------</td>
<td>-------------------------------------------------</td>
<td>-------------</td>
<td>----------------------------------</td>
<td>--------------------------</td>
<td>----------------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>55.00</td>
<td>15.00</td>
<td>74.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>20.50</td>
<td>3.00</td>
<td>30.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychology</td>
<td>Comorbid condition: Dyscognition Mood</td>
<td>Beliefs in Pain Control Questionnaire (BPCQ) ( n = 12 )</td>
<td>40.50</td>
<td>29.00</td>
<td>65.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>14.25</td>
<td>7.00</td>
<td>21.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>13.00</td>
<td>7.00</td>
<td>20.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10.00</td>
<td>6.00</td>
<td>20.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychology</td>
<td>Comorbid condition: Dyscognition Mood</td>
<td>Coping Strategies Questionnaire (CSQ) subscale ( n = 12 )</td>
<td>5.00</td>
<td>0.00</td>
<td>35.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2.00</td>
<td>0.00</td>
<td>4.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2.00</td>
<td>0.00</td>
<td>5.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychology</td>
<td>Comorbid condition: Dyscognition Mood</td>
<td>Hospital Anxiety and Depression subscale</td>
<td>8.00</td>
<td>0.00</td>
<td>12.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4.00</td>
<td>0.00</td>
<td>11.00</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Higher score = greater belief in the concept. Scores are totaled; Total possible score range 13-78; Internal locus range 5-30; Powerful doctors range 4-24; Chance happenings range 4-24.

Higher total score = higher catastrophizing (range 0-36). Total scores for other scales range 0-6.

Scores are totaled, range 0-21. Higher score shows greater rate anxiety/depression.
| Psychology | Comorbid conditions: Dyscognition | Scale (HADS) subscale | n = 12 |  |  |  | Total instrument range 28-180; higher scores = more problematic perceptions. Language range 9-45; Visual perceptual range 5-25; Verbal memory range 8-40; Visual spatial memory range 6-30; Attention/concentration range 10-50. |
|---|---|---|
| Psychology | Comorbid conditions: Dyscognition | Multiple Ability Self-report Questionnaire (MASQ) subscale | n = 11 | Total score | Language subscale | 28.00 | 21.00 | 132.00 |
| | | Visual perceptual subscale | | | 10.00 | 7.00 | 16.00 |
| | | Verbal memory subscale | | | 21.50 | 17.00 | 30.00 |
| | | Visual spatial memory subscale | | | 21.50 | 18.00 | 26.00 |
| | | Attention/concentration subscale | | | 35.00 | 33.00 | 38.00 |
| Psychology | Comorbid allied symptom: Fatigue | Patient reported outcomes measurement information system (PROMIS) Fatigue T score | n = 13 | 58.35 | 43.8 | 75.0 |
| Psychology | Comorbid allied symptoms: Sleep disturbance | Patient reported outcomes measurement information system (PROMIS) Sleep Disturbance T score | n = 13 | 54.8 | 44.8 | 76.5 |
| Psychology | Pain mechanism | PainDETECT T score | n = 13 | 12.38 | 5.00 | 38.00 |
| Psychology | Comorbid conditions: Dyscognition | Positive and Negative Affect Schedule (PANAS) subscale | n = 9 | Positive affect subscale | 34.00 | 19.00 | 44.00 |
| | | Negative affect Subscale | n = 12 | | 19.50 | 15.00 | 32.00 |
| | | | | Scores are totaled, range 10-50. Higher score shows greater rate of positive/negative affect.
<table>
<thead>
<tr>
<th>Psychology</th>
<th>Male Sexuality QOL</th>
<th>Self-esteem and Relationship Questionnaire (SEAR)</th>
<th>Total score</th>
<th>Sexual relationship satisfaction subscale</th>
<th>Total Confidence score</th>
<th>Total Confidence: Self-esteem subscale</th>
<th>Total Confidence: Relationship satisfaction subscale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social</td>
<td></td>
<td></td>
<td></td>
<td>55.51</td>
<td>49.64</td>
<td>60.95</td>
<td>72.85</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>24.90</td>
<td>15.71</td>
<td>37.14</td>
<td>64.92</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>94.29</td>
<td>94.29</td>
<td>94.29</td>
<td>94.92</td>
</tr>
</tbody>
</table>

Scores are totaled after transformation, range 0-100. Higher score is more favorable response.

Note. AUASI: American Urological Association Symptom Index; BPCQ: Beliefs in Pain Control; BPI: Brief Pain Inventory; CSQ: Coping Strategies Questionnaire; CTES/RTES: Childhood traumatic events scale/Recent traumatic events scale; HADS: Hospital Anxiety and Depression Scale; IIEF: International Index of Erectile Function; MASQ: Multiple Ability Self-report Questionnaire; M-GUPI: Male Genitourinary Pain Index; PANAS: Positive and Negative Affect Schedule; PROMIS: patient reported outcomes measurement information system (NIH); QOL: quality of life; SEAR: Self-esteem and Relationship Questionnaire; SF-12: Short Form
Table 11.

Demographics of Participants.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Result</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>48.5</td>
<td>14</td>
</tr>
<tr>
<td>Race and Ethnic Group</td>
<td>Caucasian*</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>African American</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Missing</td>
<td>1</td>
</tr>
<tr>
<td>Relationship status</td>
<td>Divorced/separated</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Unmarried couple</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Never married</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Married</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Missing</td>
<td>1</td>
</tr>
<tr>
<td>Living environment</td>
<td>Alone</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Spouse</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Parents</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Roommate</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Missing</td>
<td>1</td>
</tr>
<tr>
<td>Level of Education</td>
<td>Graduate school</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>College graduate</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Some college</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>High school graduate</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Missing</td>
<td>1</td>
</tr>
<tr>
<td>Household Income</td>
<td>&lt; 22500</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>22500-45000</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>45001-100000</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&gt; 100000</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>prefer not to say</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Missing</td>
<td>2</td>
</tr>
</tbody>
</table>

*These men also indicated non-Hispanic.
Table 12.

*Clinical information (N = 14)*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Result</th>
<th>( n )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of pain (median in months)</td>
<td>38.69</td>
<td>14</td>
</tr>
<tr>
<td>Patient reported genital site of pain</td>
<td>Right 7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Left 4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bilateral 3</td>
<td></td>
</tr>
<tr>
<td>Diagnostic studies prior to chronic male genital pain evaluation</td>
<td>Scrotal ultrasound 10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CT scan 4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MRI 3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Myelogram 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>X-ray 2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Electromyography 1</td>
<td></td>
</tr>
<tr>
<td>Interventional procedures prior to chronic male genital pain evaluation</td>
<td>Spermatic cord block 1 (helpful)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ilioinguinal block 1 (helpful)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sacroiliac joint 1 (not helpful)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cyst removal 1 (little help)</td>
<td></td>
</tr>
<tr>
<td>Family history of pain disorder</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Family history of anxiety or depression</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Family history of addiction</td>
<td></td>
<td>3</td>
</tr>
</tbody>
</table>

Table 13

*Patient-reported Medication Use (Over-the-Counter or Prescribed)*

<table>
<thead>
<tr>
<th>Medication</th>
<th>Current use ( n )</th>
<th>Past use* ( n )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibuprofen</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Tramadol (Ultram®)</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Hydrocodone and acetaminophen (Vicodin®)</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Aspirin</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Naprosyn</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Baclofen</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Cyclobenzaprine (Flexeril®)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Metaxolone (Skelaxin®)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Oxycodone and acetaminophen (Percocet®)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Propoxyphene and acetaminophen (Darvocet®)</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

*Time period not specified.*
Table 14

*Comparison of Pain Rating Scores Between Brief Pain Inventory (BPI) and PainDETECT*

<table>
<thead>
<tr>
<th></th>
<th>BPI: Average pain in last week</th>
<th>PainDETECT: Average pain in last 4 weeks</th>
<th>BPI: Worst pain in last week</th>
<th>PainDETECT: Strongest pain in last 4 weeks</th>
<th>BPI: Pain right now</th>
<th>PainDETECT: Pain right now</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median</td>
<td>4.00</td>
<td>4.00</td>
<td>7.00</td>
<td>6.00</td>
<td>4.50</td>
<td>4.50</td>
</tr>
<tr>
<td>Minimum</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Maximum</td>
<td>7</td>
<td>7</td>
<td>10</td>
<td>9</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

Table 15

*Comparison of International Index of Erectile Function (IIEF) Scores*

<table>
<thead>
<tr>
<th>Domain</th>
<th>CUO sample (median score)</th>
<th>Ciftci, et al., 2011</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 11</td>
<td>n = 50</td>
</tr>
<tr>
<td>Total score</td>
<td>55.00</td>
<td>46.0 ± 10.9</td>
</tr>
<tr>
<td>Total score:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erectile function subscale</td>
<td>20.50</td>
<td>25.3 ± 3.2</td>
</tr>
<tr>
<td>Total score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orgasmic function subscale</td>
<td>10.00</td>
<td>6.31 ± 2.2</td>
</tr>
<tr>
<td>Total score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sexual desire subscale</td>
<td>8.00</td>
<td>2.90 ± 1.0</td>
</tr>
<tr>
<td>Total score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercourse satisfaction subscale</td>
<td>9.00</td>
<td>8.58 ± 3.1</td>
</tr>
<tr>
<td>Total score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall satisfaction subscale</td>
<td>6.00</td>
<td>2.94 ± 1.4</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td>34.9 ± 7.7</td>
</tr>
</tbody>
</table>

*Note.* Total instrument range 5-75; higher score = less dysfunction. Erectile function range 1-30; Orgasmic function range 0-10; Sexual desire range 2-10; Intercourse satisfaction 0-15; Overall satisfaction range 2-10.
Table 16

Comparison of CUO Participants with Male MAPP Participants

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age</td>
<td>48.5</td>
<td>46.8 (19-82)</td>
<td>43.4 ± 15.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain duration (months)</td>
<td>38.69</td>
<td>&lt; 24 months</td>
<td>&lt; 24 months</td>
<td>93.6</td>
<td></td>
</tr>
<tr>
<td>Pain score</td>
<td>BPI 4.00</td>
<td>PainDETECT 4.00</td>
<td></td>
<td>4.9</td>
<td></td>
</tr>
<tr>
<td>AUASI total</td>
<td>6.00</td>
<td>14.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MGUPI Total</td>
<td>19.00</td>
<td>23.4 ± 7.1</td>
<td>25.5 ± 9.0</td>
<td>24.6</td>
<td>24.57 ± 8.13 n = 190</td>
</tr>
<tr>
<td>MGUPI pain</td>
<td>10.00</td>
<td>11.7 ± 3.7</td>
<td>12.6 ± 4.7</td>
<td>12.2</td>
<td>12.21 ± 4.27 n = 190</td>
</tr>
<tr>
<td>MGUPI urinary</td>
<td>1.00</td>
<td>4.2 ± 2.8</td>
<td>5.2 ± 2.8</td>
<td>4.73 ± 2.86</td>
<td>4.73 ± 2.86 n = 191</td>
</tr>
<tr>
<td>MGUPI QOL</td>
<td>8.00</td>
<td>7.58 ± 2.78</td>
<td></td>
<td></td>
<td>7.58 ± 2.78 n = 191</td>
</tr>
<tr>
<td>IIEF-6</td>
<td>55.00</td>
<td>21.4 ± 9.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HADS-D</td>
<td>8.00</td>
<td>5.2 ± 4.1</td>
<td>5.9 ± 4.1</td>
<td>5.49 ± 4.09</td>
<td>5.49 ± 4.09 n = 190</td>
</tr>
<tr>
<td>HADS-A</td>
<td>4.00</td>
<td>7.4 ± 4.4</td>
<td>7.5 ± 4.3</td>
<td></td>
<td>7.5 ± 4.3 n = 190</td>
</tr>
</tbody>
</table>

*Note. MAPP: Multidisciplinary Approach to the Study of Chronic Pelvic Pain; AUASI: American Urological Association Symptom Index; HADS: Hospital Anxiety and Depression Scale; IIEF: International Index of Erectile Function; M-GUPI: Male Genitourinary Pain Index. *Men with urologic chronic pelvic pain syndrome (UCPPC) only. + Standard deviation not reported.
Figure 7. SF-12 Report on Chronic Unexplained Orchialgia Sample. Image provided by OptumInsight Life Sciences, Inc.
Chapter 5
Discussion, Conclusions and Future Directions

This dissertation set out to examine two distinct perspectives on chronic unexplained orchialgia. The first was to explore the feasibility of a clinic dedicated to the evaluation of chronic male genital pain, with the goal of advancing clinical care. Its second purpose was to document the willingness of men to complete an extensive survey packet, and translate these results into a foundation for the clinical characterization of men with chronic unexplained orchialgia.

Limitations of the Dissertation Approach

There were acknowledged limitations to the studies conducted. The study design was exploratory and cross-sectional. Results are limited in their generalizability. For the feasibility clinic, the PI was already embedded within the general urology practice for this single academic medical center and with well-established clinical relationships. Generalizing success of establishing a Male Genital Pain Clinic to other medical center settings requires further testing. The clinic feasibility study was limited to one year, and hence sustainability is unknown. Formal cost analysis was not conducted.

For the study on characterizing men with chronic unexplained orchialgia, this study’s generalizability is also limited. It incorporated only men drawn from a single
academic medical center, with little ethnic nor racial diversity, a narrow age group, mostly urban. This was a convenience sample and with small numbers.

Despite these substantial limitations, this dissertation work does establish initial feasibility for a first clinic devoted solely to the identification of men with truly unexplained orchialgia. It raises the importance of both tangible and more intangible clinical benefits to the urology surgery faculty and the patients of a specialized nurse practitioner clinic to sort out diagnosis and treatment options for men with chronic genital pain and in particular chronic unexplained orchialgia. It provides foundational work for later full characterization of men with chronic unexplained orchialgia by careful selection of a broad array of survey instruments through a rigorous theoretical and data-driven processes. It documents adequate acceptability by these men for filling out this battery of tests.

**Recommendations**

The approach to men with chronic unexplained orchialgia introduced in this dissertation provides a natural guide to future research with this population. It provides preliminary evidence that a specialized clinic can succeed, with limited reallocation of resources within a surgical department. Additionally, it provides evidence that an expert nurse practitioner can successfully identify and manage a subtype of nonsurgical patients within urology, providing a cost-effective first point of contact (Figure 17).

Pain is the most common reason that patients seek care and the most expensive public health issue in the United States, making pain management knowledge and education vital to the role of any healthcare provider. There is a need to acknowledge and invest in specialty chronic pain populations, such as those within urology, by developing
phenotypes and algorithms, similar to those currently being pursued by the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) program, and recommended by the National Pain Strategy (IPRCC, 2015). There is a distinct benefit to categorizing and stratifying patients as a method for cost-effective evaluation and treatment. Poorly treated pain contributes to healthcare resource use, disability, and prescription drug use and abuse.

It is vital to control costs, and identifying the most appropriate provider to see particular groups of patients, especially patients who are not traditionally operative in a surgical specialty, is imperative. This means identifying the potential needs of a patient population and matching them with the provider with a complementary set of skills training. This dissertation study has shown the success that is possible with more specialized evaluation for subgroup of men, with a provider able to blend the domains of urology, pain assessment and advanced nursing with a men's health perspective.

While this pilot project represents a solid beginning to the development of a specialty practice and clinical characterization of men with CUO, the next logical step is to collect data from a larger cross-section of men, to improve the characterization and to continue to work towards a clinical phenotype. This dissertation project offers feasibility data to suggest that a possible future study design involving a large convenience sample could be successful. Inclusion and exclusion criteria will be similar to the ones for the Chapter 4 project.

Following the lead of other chronic pain conditions, research should help move clinical care to improve the interdisciplinary approach to the treatment of CUO, with the goal of improving quality of life and treatment efficacy. Investigating individual genital
pain conditions may broaden our general understanding of pain conditions and suggest alternative treatments. Qualitative clinical characterizations of men, to improve clinical understanding of the biopsychosocial and biological risk for this chronic pain condition, will also allow for better comparison with other chronic pain populations. Long-term goals with the CUO population include the creation of an evidence-based, culturally sensitive prevention and care algorithm that is consistent with the National Pain Strategy and the perspective of the Biopsychosocial Model.

**Future Research and the Biopsychosocial Model**

It is imperative to move forward and establish biological, psychological, and social factors that contribute to CUO and to promote better prevention, diagnosis, and management, as these perspectives continue to represent a significant unknown in this population. This could involve the following:

- Broadening the inclusion criteria to capture men who have episodic orchialgia or men who have other conditions such as urologic chronic pelvic pain (UCPPS) where chronic testicular pain is a component. This will help build a richer clinical characterization of men with chronic orchialgia;
- Investigation of the clinical pain experience, beyond the neurosensory component. This could include qualitative exploration of the meaning of testicular pain as relates to sexual function and an individual's perception of sexuality. Assessing the effects of chronic pain in men relative to marital or partner concerns, as well as its impact on the family and social roles, will be an important perspective of placing this pain within a biopsychosocial context. This exploration could include documentation of
men's attempts at self-management for CUO: what has been successful and how successful, before they seek to care from any provider.;

- Exploration of the biologic context of this chronic pain condition, including adding laboratory analysis in the workup of men with chronic unexplained orchialgia, including labs such as testosterone and cortisol. This could include an investigation of CUO association with other pain syndromes, especially urologic chronic pelvic pain syndrome (UCPPS), irritable bowel syndrome and other visceral pain syndromes;

- Classifying patient characteristics that predict success of specific treatments to promote cost-effective matching of patient types to treatment modalities;

- Moving toward use of quantitative sensory testing and brain imaging to investigate the potential for a central nervous system network of pathways in the pain experience that may be unique for men with CUO, or that may establish similarities with other pain populations.

**Contributions**

The following are the main research contributions of this dissertation project:

- The development of a framework that presents in organized conceptual view of men with chronic unexplained orchialgia, highlighting the gaps in knowledge and the disparity in clinical approaches to their evaluation and treatment (Chapter 2).

- The pursuit of an innovative approach to the care of a nonsurgical population of men, within an academic surgical department. This resulted in the development of a new “Chronic Male Genital Pain Clinic”. Specifically, the development of a clinic intended to provide both high-quality care, but also designed to create a platform for
the present dissertation project, and for ongoing data collection for future research on this population of men (Chapter 3).

- Synthesis of the findings from the original review of the literature (Quallich, & Arslanian-Engoren, 2013), the Biopsychosocial Model and a contemporary understanding of chronic pain, resulting in the choice of the survey instruments selected for data collection. This approach to data collection establishes the foundation for the multidimensional clinical characterization of men with chronic unexplained orchialgia (Chapter 4).

**Conclusion**

Care delivery within healthcare, and within surgical subspecialties, is changing. This research project was initially conceptualized by an expert nurse practitioner who recognizing the need to study a specific population of men in order to improve their care. An expert NP was able to independently staff a specialized men's genital pain clinic and provide an innovative and contemporary approach to the evaluation and management of CUO, a poorly described condition. This serves as a model for the utilization of an expert NP that takes full advantage of the role, knowledge, and the blended medical and advanced nursing approach. The impending shortage of trained urologists offers an opportunity for urologists and NPs to develop new strategies for care delivery, by expanding specialized clinical roles with previously marginalized populations, such as men with chronic unexplained orchialgia.
References


Table 17


In 2016, the mean, full-time base salary for an NP was $102,526.

The majority (60.7%) of NPs see three or more patients per hour.

Malpractice rates remain low; only 1.9% have been named as primary defendant in a malpractice case.

Nurse practitioners have been in practice an average of 12 years.

Over 870 million patient visits to NPs are estimated in 2016.

Average number of patients seen per day by NPs reporting a clinical focus in Urology/Nephrology: 20.2 ± 2.6.

Chronic Testicular Pain in Adult Men: An Integrative Literature Review

Susanne A. Quallich, ANP-BC, NP-C, CUNP\(^1\) and Cynthia Arslanian-Engoren, PhD, RN, ACNS-BC, FAHA, FAAN\(^1\)

Abstract
Past investigations of chronic testicular pain provide a sparse representation of the men with this condition and lack key details to aid our understanding of this important men's health condition. As a chronic pain syndrome, more research is necessary to understand the phenomenon of chronic testicular pain and the pain experience of these men. This integrative literature review provides a summary of the current state of the science of chronic testicular pain in men, identifies the gaps in our knowledge, and provides recommendations to address this knowledge gap.

Keywords
chronic testicular pain, chronic orchialgia, chronic orchialgia, men's sexual health

Introduction
Approximately 116 million American adults suffer from some form of chronic pain, costing over $635 billion each year in lost productivity and medical care costs (Institute of Medicine [IOM], 2011). The IOM recognizes chronic pain as a public health challenge that causes considerable loss of productivity and places a financial drain on the health care system (IOM, 2011). Men with chronic testicular pain (CTP) represent a small number of adults evaluated in primary care, urology (Ciftci, Savas, Yeni, Verit, & Topal, 2010), and pain clinics. Although this represents a small number of men, the impact of CTP on quality of life, social, sexual, and economic circumstances is high. In an attempt to address their chronic pain, these men are evaluated by multiple providers from different disciplines. This is congruent with the health-seeking behaviors of many other chronic pain populations, such as chronic low back pain, fibromyalgia, and interstitial cystitis (Gatchel, Peng, Peters, Fuels, & Turk, 2007; IOM, 2011; Wessellmann, Burnett, & Heinberg, 1997). CTP represents a challenging clinical entity for providers to successfully treat and manage because of its varying etiology. Oftentimes, there can be straightforward explanations for the CTP (varicocele or referred pain from an inguinal hernia), but equally often the etiology remains unexplained. In fact, from 18.6% (Ciftci et al., 2010) to 25% of CTP has no known cause (Davis, Noble, Weigel, Foret, & Mebst, 1990).

Men with CTP experience loss of economic productivity (Doubleday, Kulig, & Landel, 2003), alterations in social and family roles (Davis et al., 1990; Hong, Corcoran, & Adams, 2009), and compromises in their sexual function (Ciftci et al., 2011). Men seek evaluation from multiple providers in an attempt to uncover an explanation and treatment for their CTP (Costabile, Hahn, & McLeod, 1991; de Oliveira et al., 2009; Heidenreich, Obert, & Engelmann, 2002; Planken, Voorham-van der Zalm, Lycklama, Nijenholt, & Elzeviers, 2010).

This condition also represents a gender gap and a disparity in the knowledge for a subpopulation of men with chronic pain. There is an established body of literature that evaluates chronic pelvic pain in women (e.g., dyspareunia, interstitial cystitis, vulvodynia, vaginismus) and the sexual and social issues of these complaints (Bergeron, Rosen, & Morin, 2011; Johansen & Weidner, 2002; Wessellmann et al., 1997). As such, chronic sexual and genital pain is well detailed in women (Haefner et al., 2005). However, less is known about similar issues in the men. Findings in women with chronic genital pain recognize the need to place this pain within a psychosocial framework to evaluate not only the characteristics of the pain but also its status within the larger social and sexual context of women (Bergeron et al., 2011; Haefner et al., 2005; Mandal et al.,

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Reports of chronic genital pain conditions in men fail to evaluate their experience in this same social, sexual, and self-estem context. There is a paucity of research regarding the experience of men with CTP. Examination of this clinical entity is limited to its manifestation as a component of chronic prostatitis/chronic pelvic pain syndrome or attributed to acute conditions (e.g., epididymitis; Johansen & Weidner, 2002; Luzzi, 2005; Tripp et al., 2006).

CTP is gaining increasing awareness among men and providers, due in part to the opportunity for men to self-refer to providers, widespread availability of Internet information, and articles in gender-specific magazines (such as OQ and Men's Health) on sexual and genital health-related issues. Men are able to access information via lay publications and the Internet that confirms their experience with CTP as a valid clinical entity.

Background

Chronic orchialgia is defined as an "intermittent or constant unilateral or bilateral testicular pain three months or longer in duration that significantly interferes with the daily activities of a patient so as to prompt him to seek medical attention" (Oliver et al., 1990, p. 936). This frequently cited definition for CTP is consistent with the IOM (2011) description of chronic pain as pain lasting more than 3 to 6 months outside the realm of normal healing.

Potential causes for CTP include postvasectomy pain, epididymitis, varicocele, prostatitis, hydrocele, testicular tumor, renal colic, and referred pain from various sources (Basel et al., 2012; Rechowicz & Sullivan, 2010; Levine, 2010; Luzzi, 2003; Massani & Cox, 2003). Once identifiable causes are ruled out, a diagnosis of CTP of unknown etiology remains. Many men submit to invasive procedures to alleviate their chronic pain (vasectomy reversal, spermatic cord block, epididymectomy, denervation of the spermatic cord) with varying degrees of success (Costabile et al., 1991; Strom & Levine, 2008).

 Innervation of the testes is reasonably well explained. Autonomic supply to the male genitals originates with sympathetic fibers from the T10 and L1 vertebral segments. An additional 10% of this autonomic supply is parasympathetic and originates from the sacral S2-S4 level (Reynolds & Sills, 2007). These nerves converge, forming the spermatic plexus, which innervates the testes, epididymis, and vas deferens (Wesselsmann et al., 1997).

Somatic supply to the scrotum and testes originates from the lumbar spine L1 and L2 levels. The ilioinguinal nerve supplies sensory innervation to the root of the penis and upper scrotum, while the genitofemoral nerve innervates the cremaster muscle and parietal and visceral tunica vaginalis. S2 to S4 nerve roots innervate the posterior and inferior scrotum by way of the pudendal nerve (Rechowicz & Sullivan, 2010). This overlap in nerve supply to the testes, as well as their embryologic origin within the viscerca, may contribute to poor localization of pain to a specific scrotal structure.

Theoretical Model and Purpose

The biopsychosocial model (BPS) is frequently used to examine pain. Its origins are in general systems theory (Engel, 1982) and include the interrelatedness of systems and processes, incorporating social and psychosocial conditions within the context of medical care. Within the BPS model, an individual is seen as part of a hierarchy that recognizes distinct components as parts of a larger system (e.g., community); nothing exists alone, but has influence as a component of something larger (Engel, 1982). An advantage of this approach, especially within the context of chronic pain, is the emphasis that a particular patient complaint, although pertinent on its own, exists within a larger context of the person's history, experiences, and sensations. Furthermore, the BPS model underscores the importance that patient presentation is subject to a variety of lesser influences that might not be initially apparent (Borrell-Carrio, Suchman, & Epstein, 2004) such as social, sexual, and cultural norms. It further emphasizes the unique, subjective experience of the person. This becomes especially evident as a condition progresses from an acute to chronic state and potential economic, social, and medicolegal aspects of it become increasingly influential (Gatchel & Mayer, 2008).

The IOM (2011) recommends several parameters drawn directly from the BPS model for examination of chronic pain. These include incidence and prevalence data, a description of the characteristics of the chronic pain, its impact on daily activities, any disability related to pain, an account of utilization of services, and the costs of pain and pain care. Therefore, the purposes of this integrated literature review are to describe what is currently known about men with CTP, to identify the gaps in the state of the science, and to provide recommendations for future research. To this end, we will describe the current definition of CTP, the scope of the problem, and present a review of studies addressing this important aspect of men's health.

Method

We conducted a search of the published literature from January 1970 to September 30, 2012, using the following databases: Google Scholar, MEDLINE, CINAHL, ProQuest, PSYCHINFO, Web of Science, and SCOPUS. The search was limited to articles with the following key words in their titles: testicular pain, chronic orchialgia, chronic testicular pain, chronic testalgia, chronic scrotal pain, chronic male genital pain, chronic orchidalgia, and
chronic orchialgia. These terms were further narrowed by excluding children and selecting subjects at least 18 years of age. Only articles available in English were reviewed. Review articles, published abstracts, citations, letters to the editor, commentaries, patents, book chapters, and animal studies were excluded. Articles that included discussion of CTP with an identified cause, such as malignancy or postvasectomy pain, were also excluded. This resulted in a total number of 15 research-based articles and 11 case reports (Figure 1).

Exclusion and inclusion criteria used in this review resulted in the purposeful exclusion of one of the most frequently cited articles discussing CTP (Davis et al., 1990). We chose to exclude this article for two reasons: it includes children as young as 11 years (range = 11-69) and because it contains no details regarding the number of participants below the age of 18 years. It is likely that the etiology and experience of CTP in adolescent and preadolescent boys is different from that of adult men. Its interpretation and evaluation requires an understanding and appreciation of their chronological age and development. We also excluded two other articles (Perimenis, Speckman, & Higgins, 1994; van Haarst, van Andel, Pels Rijcken, Schatmann, & Taconis, 1999) because of the young age of subjects (14 and 10 years, respectively).

**Results**

A total of 28 were reviewed (15 research articles, 11 case studies). A consistent definition of CTP is noted among the articles reviewed, based on the Davis et al. (1990) definition. The research articles are predominantly retrospective chart reviews, with the largest cohort evaluating 71 men (Benson, Abern, Larsen, & Levine, 2012). A summary of the research studies (Table 1) and case studies (Table 2) is presented.

**Biological Aspects**

Pain ratings for article are by self-report, and only one article describes an intervention that included a control group (Ciftci et al., 2011). Little is known about demographic characteristics of these populations beyond age. Although age is consistently reported, other demographic information is not. Only Costabile et al. (1991) reports the racial composition of their sample (88% Caucasian; 10% African American). A complete workup to rule out identifiable causes for CTP is mentioned, but the precise nature of any workup is not detailed, and the focus is primarily on success or failure of invasive treatments or surgical interventions. Pain description is limited to its location in the scrotum (left, right, bilateral) without localizing it distinctly to the testis. A visual analog scale is used to measure intensity. Only three of the research articles (Ciftci et al., 2011; de Oliveira et al., 2009; Misra, Ward, & Coker, 2009) and four of the case reports (McJunkin, Woullet, & Lynch, 2009; Nouri & Brish, 2011; Rosendal, Moir, de Pennington, Green, & Aziz, 2012; Rowell & Rylander, 2012) include the quality of CTP.

Sinclair, Mikes, and Lee (2007) offer support for a neuropathic origin of CTP and are the first to show that neurmodulating medications decrease pain in chronic orchialgia. This is consistent with reports that describe the pain as shooting, gnawing, or sickening (Misra et al., 2009), terms often used to describe neuropathic pain. Pathological evaluation suggests inflammation, obstruction, or ischemia may be contributing factors to the chronic pain experience (Nuriculam, Minh, Adeniyi, Ralph, & Freeman, 2007).

Many of the descriptors within the case studies are consistent with descriptions of neuropathic and radicular-type referred pain. The pain is described as “sharp, shooting” (McJunkin et al., 2009), “burning, stabbing, with radiation”
<table>
<thead>
<tr>
<th>Reference and country</th>
<th>n</th>
<th>Age range (mean)</th>
<th>Methods</th>
<th>Standardized tools</th>
<th>Intensity</th>
<th>Quality</th>
<th>Location</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costabile et al. (1991), the United States</td>
<td>46</td>
<td>29-68 (45)</td>
<td>Retrospective and prospective chart review</td>
<td>Serum/testes</td>
<td>~11 months</td>
<td></td>
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<tr>
<td>Yanase et al. (1995), Japan</td>
<td>12</td>
<td>24-41</td>
<td>Retrospective and prospective chart review</td>
<td>Left side: 4</td>
<td>&gt;3 months</td>
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<td>Right side: 6</td>
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<tr>
<td>Levine, Mackay and Lubenow (1996), the United States</td>
<td>7</td>
<td>36-59 (45.6)</td>
<td>Retrospective review: mean between June 1991 and September 1994</td>
<td>Bilateral 2</td>
<td>85 months</td>
<td></td>
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<td></td>
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<td></td>
<td>Bilateral 1</td>
<td>10-237 months</td>
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<td></td>
<td>Unilateral 6</td>
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<tr>
<td>Cadeddu et al. (1999), the United States</td>
<td>9</td>
<td>26-47 (37.7)</td>
<td>Retrospective chart review: mean between December 1999 and October 1998</td>
<td>Analog pain scale (0-100)</td>
<td>Before treatment 69.4 (35-90); after treatment 30.6 (0-90)</td>
<td>49 months (12-180 months)</td>
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<td></td>
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<td></td>
<td>Bilateral 6</td>
<td>5-360 months</td>
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<td></td>
<td></td>
<td>Unilateral 21</td>
<td></td>
<td></td>
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<tr>
<td>Heldenscheidt et al. (2001), Germany</td>
<td>25</td>
<td>45.9 at surgery (5.8-54)</td>
<td>Long-term follow-up data</td>
<td>Bilateral 2</td>
<td>10-280 months</td>
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<td></td>
<td></td>
<td></td>
<td>50% with complete resolution after surgery</td>
<td>36 months (3-72)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Pain scale 0-10</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Pain before treatment 8.5</td>
<td>17 months (2-16 months)</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>6 posttreatment</td>
<td>62 months (5-252 months)</td>
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<td></td>
<td>Bilateral 16</td>
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<td></td>
<td>Unilateral 63</td>
<td>40 months (3-73 months)</td>
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<td></td>
<td>Continuous or intermittent</td>
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</tbody>
</table>

(continued)
Table 1. (continued)

<table>
<thead>
<tr>
<th>Reference and country</th>
<th>n.</th>
<th>Age range (mean)</th>
<th>Methods</th>
<th>Standardised tools</th>
<th>Pain characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mora et al. (2009), the United Kingdom</td>
<td>10</td>
<td>22-65 (69 ± 10)</td>
<td>Prospective uncontrolled pilot study of pulsed radiofrequency of spastic cord form September 2005 to December 2006</td>
<td>VAS</td>
<td>Before treatment: VAS: 7.1 (4.3-8.7) VAS: 3 months after: 4.2 (0.6-9.8)</td>
</tr>
<tr>
<td>Ofci et al. (2010), Turkey</td>
<td>113</td>
<td>18-55 (32.5 ± 10)</td>
<td>Prospective evaluation, all men who came to clinic between March 2007 and June 2007</td>
<td>0-10 pain scale</td>
<td>Right curvature: 45% Left curvature: 10% Bilaterally: 19%</td>
</tr>
<tr>
<td>Planken et al. (2010), Netherlands</td>
<td>41</td>
<td>23-81 (48)</td>
<td>Retrospective study</td>
<td>DPPF</td>
<td></td>
</tr>
<tr>
<td>Ofci et al. (2011), Turkey</td>
<td>50 men, 50 controls</td>
<td>Pain men (34.9 ± 7.7 years) Controls (37.6 ± 4.9 years)</td>
<td>Prospective study to evaluate effect of chronic sexual pain on sexual function</td>
<td>IIEF</td>
<td></td>
</tr>
<tr>
<td>Benson et al. (2012), the United States</td>
<td>74</td>
<td>17-74 (42)</td>
<td>Retrospective review</td>
<td>VAS pain scale from the McGill Pain</td>
<td>Mean before cord block: 8 (5-10) Mean after surgery (doesnt taste how long): 2 (0-10)</td>
</tr>
</tbody>
</table>

Note: DPPF = standard Dutch evaluation of pelvic floor function that includes the Pelli's history tool and electromyography; IIEF = International index of erectile function; WHOQOL-Brief = World Health Organization Quality of Life questionnaire-Brief; VAS = visual analog scale.

### Table 2. Case Studies/Series Evaluating Chronic Testicular Pain

<table>
<thead>
<tr>
<th>Reference and country</th>
<th>n</th>
<th>Age</th>
<th>Standardized tools</th>
<th>Intensity</th>
<th>Quality</th>
<th>Location</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Devine and Schellhammer (1978), the United States</td>
<td>2</td>
<td>Both 42</td>
<td></td>
<td></td>
<td></td>
<td>Case 1: Bilateral and intermittent</td>
<td>Case 1: &gt;30 months</td>
</tr>
<tr>
<td>Choa and Swami (1992), the United Kingdom</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Case 2: Right testis with radiation to right inguinal area</td>
<td>Case 2: 84 months</td>
</tr>
<tr>
<td>Jemilek et al. (1992), Czechoslovakia</td>
<td>10</td>
<td>30-55</td>
<td></td>
<td></td>
<td></td>
<td>Pain disappeared in 100% of participants after program of manual manipulation</td>
<td>&gt;18 months</td>
</tr>
<tr>
<td>Doubleday et al. (2003), the United States</td>
<td>1</td>
<td>36</td>
<td>Oswestry Disability Index (ODI)</td>
<td></td>
<td></td>
<td>Right upper buttock</td>
<td>60 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Right testicular pain (inconsistent)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Right leg paresthesia</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Unable to run, sit for long periods or lie flat; slept in recliner</td>
<td></td>
</tr>
<tr>
<td>McJunkin et al. (2009), the United States</td>
<td>1</td>
<td>31</td>
<td>Pain scale</td>
<td>Average pain pretreatment: 8/10</td>
<td></td>
<td>Sudden onset right testicular pain—epididymitis that became constant</td>
<td>~144 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Average pain posttreatment: 2-4/10</td>
<td></td>
<td>Sharp, shooting</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Worse when moving to standing, coughing, lifting, or with sexual activity</td>
<td></td>
</tr>
<tr>
<td>Nairn and Ende (2011), Australia</td>
<td>5*</td>
<td>24.75</td>
<td>Prospective evaluation of short-term psychological and emotional therapy (journey therapy)</td>
<td></td>
<td></td>
<td>Various descriptions with little actual anatomic detail</td>
<td></td>
</tr>
</tbody>
</table>

(continued)
<table>
<thead>
<tr>
<th>Reference and country</th>
<th>n</th>
<th>Age</th>
<th>Standardized tools</th>
<th>Pain characteristics</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nouri and Brisht (2011), the United States</td>
<td>1</td>
<td>57</td>
<td>VAS</td>
<td>Intensity: 5/10, Quality: Burning, Stabbing</td>
<td>24 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Location: Left scrotum, with radiation to left inguinal area</td>
<td></td>
</tr>
<tr>
<td>Rosendal et al. (2012), the United Kingdom</td>
<td>1</td>
<td>30</td>
<td>VAS</td>
<td>Intensity: Before: 9/10, After: 3/10, Quality: Constant</td>
<td>36 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Location: Left, with radiation to perineum, low back, abdomen</td>
<td></td>
</tr>
<tr>
<td>Basler et al. (2012), Turkey</td>
<td>5</td>
<td>Average 29</td>
<td>Case series VAS</td>
<td>Intensity: 3 weeks before treatment: mean VAS: 9, 3 weeks after treatment: mean VAS: 1</td>
<td>7.8 months (5-12 months)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Quality: 3 left, 1 right, 1 bilateral</td>
<td></td>
</tr>
<tr>
<td>Rowell and Rylander (2012), the United States</td>
<td>1</td>
<td>36</td>
<td>Case report, Pain rated by 0-10 scale via NRS for low back pain Oswestry Disability Index (ODI)</td>
<td>Pain: Before treatment: 6/10, After treatment: 0/10, Quality: Sudden onset “Constant dull ache that never remitted”</td>
<td>~60 years</td>
</tr>
<tr>
<td>Tu et al. (2012), China</td>
<td>1</td>
<td>47</td>
<td>VAS (0-10), SAS (Self-Rating Anxiety Score), Self-Rating Depression Scale (SDS)</td>
<td>Intensity: Before treatment: 8/10, SDS: 0.55, SAS: 46, After treatment: 0/10, SDS: 0.50, SAS: 42</td>
<td>~80 months</td>
</tr>
</tbody>
</table>

Note: VAS = visual analog scale.
a. For some articles, total n was higher than what is listed; only cases that remained unexplained are included in the table.
(Nouri & Brish, 2011), “continuous, sharp, with radiation and hyperesthesia” (Rosendal et al., 2012), “incapacitating” (Choa & Swami, 1992), and as a “constant dull ache” (Rowell & Rylander, 2012). Central vertebral disc protrusion, thoracolumbar dysfunction, muscle spasms, or sacroiliac joint dysfunction (Doublingay et al., 2003; Jemelik, Penickova, & Vyborny, 1992) is documented in men with CTP, offering a potential pathophysiological etiology for their complaints of neurologic pain sensations.

**Psychological Aspects**

Additional aspects of the impact of CTP are poorly reported in the articles reviewed. Cifci et al. (2011) use standardized tools to establish that CTP reduces quality of life, sexual satisfaction, frequency of sexual activity, and overall libido when compared with controls.

CTP may be a unique manifestation of chronic pelvic floor dysfunction, a result of possible sexual abuse, or may be related to chronic pelvic pain syndrome (Planken et al., 2010). Costabile et al. (1991) suspect a precipitating event prior to a diagnosis of CTP, although no specifics are provided. When this aspect is explored, men become “angry and incredulous when it is suggested they may benefit from referral to a mental health professional” (Cadeddu et al., 1999, p. 734).

The case studies in this review offer insight into a possible psychogenic component of CTP. In the original article describing microsurgical denervation of the spermatic cord, DeVine and Schellhammer (1978) report that one of their patients had “recurrent pain . . . due to an overriding psychogenic component” (p. 151). Naim and Ende (2011) report the identification of deep-seated emotions resulting in chronic genital and testicular pain.

**Social Aspects**

Only 3 of the 15 research studies address the issue of work status, educational level, or the potential economic impact of CTP. Costabile et al. (1991) note that 30% of the Army population in their study completed some level of college, 20% had professional-level jobs, 31% were skilled laborers, and 42% were manual laborers, but the impact of CTP on their ability to function at their jobs remains unclear. However, 31% (15/48) were eventually granted medical discharge due to their chronic orchialgia. Treatment with pulsed radiofrequency of the spermatic cord allowed 10 men to resume normal activities (Miara et al., 2009). Cadeddu et al. (1999) speculate that men resort to surgery in part due to limited insurance coverage for physical therapy and mental health services.

The economic impact of CTP on the work status of these men is unclear; not all men were working when evaluated as subjects of the case studies. However, after treatment many are able to return to work (Doublingay et al., 2003; McJunkin et al., 2009; Nouri & Brish, 2011; Rosendal et al., 2012).

**Discussion**

Based on the 26 articles in the review, the characteristics of the average man with CTP is a 45-year-old, Caucasian of European descent, and has suffered CTP for 3 to 366 months (Benson et al., 2012; Nariculam et al., 2007). The pain is more likely to be unilateral and slightly more likely to be on the right side of the scrotum. Various and numerous conservative treatment measures have failed; he has seen on average 4.5 urologists (Heidenreich et al., 2002), has undergone 4.7 to 7.2 procedures (Costabile et al., 1991; Heidenreich et al., 2002), and has had 1.6 surgeries (Costabile et al., 1991).

The estimated prevalence of chronic scrotal pain is 4.75% of all men presenting to urology clinics, with up to 18.6% of these men never receiving a satisfactory explanation for the cause of their pain (Cifci et al., 2010). However, the incidence of CTP remains elusive, as chronic testicular pain is likely to incorporate CTP. The absence of specific precipitating events clouds the issue, yet for a considerable number of men the primary treatment focuses on coaching to encourage “changes in their perception and coping mechanisms” for this chronic pain condition (Costabile et al., 1991, p.1572).

**Biologic Considerations**

A precise cause for complaints of chronic scrotal or testicular pain is difficult to ascertain due to the inconsistent use of descriptors throughout the literature. The terms testicular pain, chronic testicular pain, chronic scrotal pain, chronic orchialgia, chronic orchialgia, chronic orchaidynia, and chronic genital pain have been used interchangeably to describe complaints of chronic pain to the male scrotum. In an attempt to provide clarity, Levine (2010) offers the term chronic scrotal contents pain to capture the phenomenon of chronic pain that occurs in any portion of the scrotum or its contents, including the testicle, testicular accessory structures, spermatic cord, epididymis, or the scrotal skin itself. This umbrella term, however, fails to adequately acknowledge the differences in innervation among these structures and may make classification of this chronic pain syndrome more complicated. Furthermore, it may perpetuate imprecision in identification of the precise nature and location of the pain. This potential inaccuracy is reflected in current algorithms, which do not recommend psychological or
psychiatric evaluation (Benson et al., 2012; Benson & Levine, 2012) that may aid in the discrimination of the pain and uncover other contributing factors such as somatization (Hong et al., 2009).

The reviewed studies of CTP fall short of the current IOM recommendations regarding assessment of pain. Many fail to use standardized tools to capture characteristics of pain, with the exception of a pain scale. When incorporated, pain scales are inconsistently used among these studies. Some studies use a 0 to 10 scale, whereas others use a 0 to 5 scale, making comparisons difficult.

Assessment of pain should include investigation of its multiple dimensions (intensity, quality, location, duration, and sites other than a primary site) (IOM, 2011). The case studies provide a more rich and detailed description of the chronic pain experience of these men, including a much better description of pain quality and precise location(s) of the pain.

The review of the literature reveals that little is known about the demographics of men with CTP beyond age. This lack of demographic data significantly limits our ability to understand the potential influence of sexual orientation, ethnic, social, and cultural variables on CTP and hampers our ability to recognize at-risk men for developing CTP. Understanding the social and cultural norms that influence men and their response to CTP, while establishing a potential pain phenotype for this condition, is very difficult given the limited information.

**Psychological Considerations**

To date, very little attention is focused on the psychosocial aspects of the chronic pain experience for men with CTP, despite the existing model available for parallel conditions in women (Haefner et al., 2005; Mandal et al., 2010). The intensity of pain alone provides inadequate insight into the effects of pain on an individual. This limited knowledge hinders comparison across the studies as well as among other groups of chronic pain patients. It also ignores the extent to which pain and anticipation of pain may result in avoidance and other maladaptive behaviors.

Furthermore, the literature review reveals a lack of research on predicting factors that contribute to CTP and disability in men. This may represent a failure of current medical treatment or a lack of recognition of the emotional suffering and poor quality of life that bring men back to providers or specialty clinics for evaluation and treatment (Kumar, Mehta, & Nargund, 2010). Psychological or psychiatric evaluation is not a priority within current recommendations for treatment. Psychological evaluation may be considered prior to certain invasive surgical procedures (Davis et al., 1990), such as orchectomy, but this option is not reflected in contemporary algorithms (Benson et al., 2012; Benson & Levine, 2012). Within the parameters of the BPS, it would be prudent to evaluate psychological status prior to less invasive treatments, as psychological factors can influence the overall experience of pain (Gatchel, 2004; IOM, 2011).

Men with CTP demonstrate characteristics found in other chronic pain syndrome patients, such as reporting pain as their chief complaint, low correspondence between symptoms and objective medical findings, an association with psychosocial dysfunction, and a history of multiple, unsuccessful treatments (IOM, 2011; Kumar et al., 2010; Planken et al., 2010). This includes a "try anything" attitude that results in "an extraordinary number of interventions" (Egan & Krieger, 1997, p. 215) usually with a low success rate. This is consistent with somatization disorders. Standardized instruments for general assessment of somatization disorders may not be reliable and valid in men with CTP, supporting the premise that psychological and psychiatric evaluation be conducted prior to invasive procedures (Hong et al., 2009).

Some men with CTP have pain secondary to sexual abuse. Four articles suggest there may be a component of sexual abuse in some of these men (Costable et al., 1991; Davis et al., 1990; Planken et al., 2010; Schover, 1990).

The Schover (1990) pilot study describes 48 men who underwent a psychological interview after being referred by urologists who could not establish an organic cause for their genital pain. These white-collared men tended to be Caucasian (90%) with a mean age of 41 years, with poor social support, significant life stressors, and evidence of possible somatization disorders (56%). Major depression (27%) and chemical dependency issues (27%) were also noted. Psychological distress about sexual inadequacy and loneliness prevented intimacy, whereas complaints of pain were seen as a strategy to elicit attention from health care professionals and social contacts. Schover concluded that stress-induced chronic muscle tension creates pain and advises against labeling the pain in psychological terms. In most subsequent studies, this psychological aspect is not studied. Schover investigates chronic genital pain complaints, not specifically testicular pain, but this article guides much of the subsequent conceptualization of the CTP population.

**Social Considerations**

Despite the known impact of chronic pain on lost productivity and medical care costs, the economic impact of CTP is rarely cited in the literature. There is almost no mention of it as it relates to work status prior to treatment or as it relates to the ability to return to work posttreatment. This creates a challenge in drawing conclusions regarding the true economic impact of this condition. There are ample
data indicating that the economic impact of chronic pain is significant, regardless of the site of pain. IOM (2011) data indicates that the annual cost to the health care system is $4,516 more per individual with moderate pain and $7,726 more per individual with severe pain when compared with an individual without pain.

Limitations
There are two limitations of this review. First, it did not include children, which may limit our overall understanding of CTP. However, as CTP in children is most likely a distinct clinical entity, limiting our review to adult men helps establish the parameters unencumbered by issues related to growth and development. Second, only chronic unexplained testicular pain was examined. Although the inclusion of CTP with identifiable causes would have increased the overall pool of studies, we chose to focus on CTP without identifiable causes to shed light on this elusive area of study.

Future Directions
Given the paucity of studies describing men with CTP, there is a desperate need for data describing this area of men’s health and its impact on men and their families. Demographic data are needed to characterize men affected by CTP, including socioeconomic status, sexual orientation, ethnicity, relationship status, and past medical and surgical history. Information detailing types of providers who are associated with various treatment options is also needed and may include primary care providers (including nurse practitioners and physician assistants), urologists, neurologists, psychologists, and anesthesiologists.

Because contemporary literature lacks psychological description of the experience of CTP, qualitative research is needed to uncover the key aspects of what it is like to live with this debilitating chronic pain condition. An increasing body of literature demonstrates that individuals living with chronic pain tend to catastrophize their pain experience, resulting in specific bodily complaints (Edwards, Bingham, Bathon, & Haythornthwaite, 2006; Gatchel, 2004; IOM 2011; Seminowicz & Davis, 2006). It is reasonable to conclude that some men with CTP may also catastrophize their pain. If so, this has implications in terms of their overall CTP experience, as the cognitive interpretation of pain can give rise to physiological and behavioral responses that influence an individual’s performance outcomes and create a more intense pain experience and increase emotional distress (Gatchel et al., 2007; Jensen, 2010). Catastrophizers have difficulty directing their attention away from pain and succumb to rumination, feelings of helplessness, and pessimism regarding outcomes, all of which predict higher self-reported disability (Edwards et al., 2006; Seminowicz & Davis, 2006). The IOM (2011) specifically recommends screening for this characteristic as a predictor of treatment success, as it predicts future disability scores after controlling for variables such as gender and type of pain syndrome (Karoly & Ruchhman, 2007; Sullivan et al., 2001).

In addition, catastrophizing may also represent a broader dimension of maladaptive coping for men with CPT, providing dysfunctional feedback and increasing the pain experience. This method of coping may represent an attempt to ensure that pain is dealt with externally rather than addressing the individual’s internal cognitive environment (Sullivan et al., 2001) and is consistent with the findings of Schover (1990), who concluded that pain was a strategy to create attention. To evaluate catastrophizing, the Pain Catastrophizing Scale should be administered and considered a primary screening tool. It may become possible to predict who is less likely to respond to traditional medical and surgical treatments, if there is strong evidence for catastrophizing. Further investigation of this particular aspect of chronic pain may make it possible to propose treatments for men with CTP that have been successful with other chronic pain groups that catastrophize.

Additionally, standardized tools should be incorporated into the study of CTP to capture its multiple facets, as noted in the BIPS, to direct future interventions to manage, control, and treat CTP. These measures include overall coping, symptom perception, and pain-related disability and not simply questions regarding the presence or absence of pain or genitourinary symptoms. Instruments such as the Somatization subscale of the Symptom Checklist-90-Revised, Mcgill Pain Questionnaire, the Perceived Stress Scale, the Brief Sexual Functioning Questionnaire, the Survey of Pain Attitudes, the Short Form-36, the Multidimensional Scale of Perceived Social Support, and the Chronic Pain Coping Inventory may be beneficial. A “pain map” (schematized picture of the male genitalia) may also be helpful in determining the precise anatomic location of pain. These tools have been widely used with other chronic pain populations (Edwards et al., 2006; IOM, 2011) and would allow for comparison between men with CRTP and other chronic pain patients.

Conclusions
The current state of the science regarding CTP is underdeveloped and incomplete; the characteristics of men affected by CTP are poorly described, as are consistently effective treatments and interventions. The three most cited studies (Costabile et al., 1991; Davis et al., 1990;
Schover, 1990) are more than 20 years old and consist of a combination of retrospective and prospective chart review without the inclusion of standardized psychometric tools. Additional research is urgently needed to address this poorly studied condition affecting the quality of life for men and their families.

Declaration of Conflicting Interests
The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding
The authors received no financial support for the research, authorship, and/or publication of this article.

References
Appendix B
Building a Clinic Infrastructure

In order to aim for efficiency in data collection of men with chronic orchialgia several system and infrastructure steps were necessary. It was simply not practical for the principle investigator to review the daily schedules of dozen providers and plan to be in any one of the six adult urology clinic sites to try and approach men to participate in my dissertation project. Since men with chronic genital pain complaints are typically challenging patients within the normal pace of the clinic schedule, it became clear that the most efficient manner for capturing these patients for potential participation in this CUO feasibility my study would be to designate particular clinics exclusively for chronic male genital pain referrals and follow-up.

1. The plan to create a new clinic was discussed with the collaborating physicians. They approved of this proposal, realizing that not only would it help streamline their own clinic populations, but provide a service to these men by scheduling them with the provider who had both interest and the skills to give them a thorough evaluation.

2. The plan was then presented to the clinical manager, for discussion and additional input. The proposal was for this new male genital pain clinic to take the place of a regularly scheduled clinic, since the principle investigator would be the primary provider evaluating these patients. This had the added benefit of not requiring either additional clinic space or additional support staff, as the clinic time was already designated for patients scheduled with the principle investigator.

3. A set of referral criteria for the “Chronic Male Genital Pain Clinic,” including consult request guidelines that would be available to referring providers outside the University of Michigan Health System, was created. The collaborating physicians were approached for input. These guidelines were based on both expert opinion and the best available information pulled from the literature for the preliminary workup of men with chronic male genital pain.
4. The next step was to contact providers who had previously accepted these diagnoses (testicular pain, scrotal pain, penis pain, groin pain, or epididymal pain > 3 months) to see if they would be willing to allow an alteration in scheduling, so that all of these referrals would automatically be scheduled into the new clinic. Support of this endeavor was unanimous, and there were no providers who wished to retain referrals.

5. In order to try and capture referrals for chronic male genital pain to the adult urology department, it was necessary to review the diagnoses lists for each provider by hand in order to identify both physicians and mid-level providers who were currently accepting men with complaints of chronic genital pain.

6. The principle investigator with the clinic manager on several occasions in order to design and have her eventually construct the scheduling grid for this clinic.

7. Once the scheduling grid was set, the diagnoses from all other providers in the adult urology departments could be combined to ensure that referrals for chronic male genital pain would be directly scheduled into this new clinic. This involved turning over the master list of providers and their list of diagnoses to the adult urology call center staff, in order to remove the chronic male genital pain diagnoses from all other providers, and facilitate automatic scheduling into the new Chronic Male Genital Pain Clinic.

8. Because of the unclear number of referrals for these issues to the department, coupled with the inability to accurately capture the number of these men that had been previously seen due to nonspecific ICD coding for this condition, there was no estimate for the number of men that could be anticipated as referrals in any given time. Because of this fact the clinic, was initially set up to run every other Tuesday, beginning mid-June 2015.

9. Scheduling staff were instructed to contact the principle investigator directly with any questions about the appropriateness scheduling referral into this new clinic.
10. The initial six weeks after this clinic opened saw very few men who were scheduled. This was initially attributed to summer, when overall clinic attendance for non-urgent andrology issues can be slower.

11. However, as few men continued to be scheduled into these new clinics, the principle investigator contacted the call center to make sure that the necessary changes had been made to the master scheduling guidelines. At this point it became clear that the diagnoses lists had not been collapsed and that men referred for chronic genital pain were continuing to go to multiple providers and to various clinical sites within the department.

12. A meeting was scheduled between the call center staff and principle investigator to review the referral criteria, and to emphasize that all other providers had agreed to this change in schedulings for chronic male genital pain, and encourage them to be scheduled in the new Chronic Male Genital Pain Clinic.

13. During this period of time there were multiple informal meetings with the clinic manager, trying to work through solutions that would allow for better utilization of this clinic.

14. The principle investigator was also able to make providers within the Department of Urology aware of this clinic. This started a pattern of internal referrals for chronic male genital pain for men that had previously been evaluated by other adult urology providers.

15. Fall of 2015 saw a slow and gradual increase in utilization of these new clinics, and the pace of consenting men for the CUO study increased.
Appendix C
Summary of Instruments Used for Cross-sectional Study

American College of Rheumatology Diagnostic Criteria for Fibromyalgia (ACR criteria)

The American College of Rheumatology diagnostic criteria for fibromyalgia was originally offered in 1990 (Wolfe, et al., 1990) and revised in 2010 (Wolfe et al., 2010). The instrument includes a pain map, a symptom severity scale score and somatic symptom score. Higher scores indicate worse symptomatology or increased body system involvement; the wide spread in his score for pain can range from 0 to 19 with a higher score indicating the involvement of more body locations. The symptom severity score ranges from 0 to 12 and this summed score includes an estimation of the number of associated somatic symptoms. The 2010 revision shifted the definition toward a more clinically useful classification for fibromyalgia, or centrally mediated pain, cases.

American Urological Association Symptom Index (AUASI)

The American Urological Association Symptom Index (AUASI) was developed to address the urinary symptoms reported with benign prostatic hyperplasia in clinical populations (Barry et al., 1992; Chai et al., 1993). Higher scores indicate worse symptom bother, and the instrument is scored according to well-established range for little bother intermediate bother and general bother.

Beliefs in Pain Control Questionnaire (BPCQ)

The Beliefs in Pain Control Questionnaire was developed to standardize invalid scale to measure beliefs about controlling pain in both clinical and nonclinical settings
(Skevington, 1990; Skevington, 1991). It provides a meaningful assessment of beliefs about pain control, whether there is an internal or external locus of control.

**Brief Pain Inventory (BPI) for Males**

The Brief Pain Inventory (BPI) measures the participant subjective interpretation of his pain developed in 1994 (Cleeland & Ryan, 1994). A higher score indicates more severe pain and greater pain-related interference. Its two-factor structure has been shown to be consistent (Cleeland, 2009) across cancer pain population and nonmalignant chronic pain patients. There has been less investigation of the factor structure reliability in nonmalignant chronic pain populations. For this study, the male specific form (BPI-M) of the instrument was used, which includes a male genital map for participants to indicate the site(s) of their pain.

**Six-item Catastrophizing Sub-scale from Coping Strategies Questionnaire (CSQ)**

The Coping Strategies Questionnaire (CSQ) (Hirsh, George, Riley, Robinson, 2007; Rosenstiel, & Keefe, 1983) measures patients’ use of pain coping strategies; only the items from the catastrophizing sub-scale were chosen for this project, to maintain a parallel structure with the MAPP project. Higher scores indicate higher catastrophizing, and may translate into higher pain scores.

**Childhood Traumatic Events Scale/ Recent Traumatic Events Scale (CTES/RTES)**

This instrument is composed of two forms one that investigates childhood trauma before age 17 and one that investigates traumatic events in the last three years (Pennebaker & Susman, 1988). Both measure similar domains including death of a close family member, serious illness, and sexual assault. Participants are asked to rate their experiences on a six-point Likert scale The instrument is scored based on individual
items, or totaled for some across all traumas, and asks if participants confided about the trauma.

**Hospital Anxiety and Depression Scale (HADS)**

The Hospital Anxiety and Depression Scale was developed in 1983 (Snaith & Zigmond, 1986; Zigmond & Snaith, 1983). HADS is designed to screen for anxiety and depression (in patients with physical health problems. Items were selected to provide for the greatest distinction between anxiety and depression, while excluding items that might reflect somatic symptomatology. Scoring of the instruments has been clearly established: 0 to 7 indicates no anxiety or depression; 8 to 10 suggests anxiety or depression; 11 to 21 indicates anxiety or depression. Higher scores on this instrument indicate higher distress.

**International Index of Erectile Function (IIEF)**

This instrument was developed specifically to assess erectile function by patient self-report and was designed to be sensitive to treatment changes (Rosen, et al., 1997; Rosen, 1998). It evaluates five separate domains of sexual function and is consistent with the NIH definition for erectile function, and was designed to meet the needs of regulatory agencies across the world (Rosen, Cappelleri, & Gendrano, 2002).

**Multiple Ability Self-report Questionnaire (MASQ)**

The Multiple Ability Self-report Questionnaire (MASQ) was developed in 1994 (Seidenberg, Haltiner, Taylor, Hermann, & Wyler, 1994). Higher scores equal a greater degree of self-reported cognitive difficulty. To date it has unclear validation specifically in men with chronic pain.

**Male Genitourinary Pain Index (M-GUPI)**
The Male Genitourinary Pain Index is a 10 item instrument designed specifically to measure genitourinary pain in men (Clemens, et al., 2009). The total score ranges from 0 to 45, with a higher score indicating worse symptoms. It measures three factors: pain, urinary symptoms, and quality of life. It has been validated specifically in men with genitourinary pain diagnoses and is an integral instrument in the NIH MAPP study.

**PainDETECT**

This instrument uses the IASP taxonomy for the definition of neuropathic pain: “pain resulting from a lesion or dysfunction of the peripheral or central nervous system”. It was developed in 2006 (Freynhagen, Baron, Gockel, & Tölle, 2006) after review of the literature to determine factors relative to the patient experience of neuropathic pain syndromes. Responses less than or equal to 12 indicate an unlikely neuropathic component to pain, while results greater than or equal to 19 indicate a likely neuropathic component. Responses that fall in between this range indicate a physical examination is required for diagnosis. Since its original development, a body chart or body map has been included.

**Positive and Negative Affect Schedule (PANAS)**

The Positive and Negative Affect Schedule (PANAS) was designed to measure subjective distress and positive emotionality (Watson, Clark, & Tellegan, 1988). It has been validated both clinical and nonclinical populations (Crawford & Henry, 2004), and have been proven to be stable in a variety of time frames. Higher scores on the positive affect items reflect higher levels of positive affect, while lower scores on the negative affect scale reflect lower levels of negative affect.

**PROMIS Instruments**
In 2004, the NIH began its Patient Reported Outcomes Measurement Information System (PROMIS) initiative with the goal of establishing a framework and items for a set of both adult and pediatric item banks. The PROMIS network used a modified Delphi approach, multiple rounds of framework review and revision to create domains and items for specific domains (Cella, et al., 2010; Cella et al., 2007). Existing legacy outcome questionnaires created the initial item bank for the NIH steering committee to use in their selection of specific items that would eventually comprise the new questionnaires. Items from well-established, well-validated psychometric instruments were subjected to a rigorous literature review to choose items that fit the specific domain definitions that had been chosen. PROMIS workgroups sorted through thousands of items according to content and decided which items were most representative of their individual domains. Resulting items were subject to expert review and revision, with specific attention paid to content, clarity and readability. The resulting panel of items were subjected to two waves of testing, resulting in calibrated item banks, most of which utilize a seven-day recall period. The resulting PROMIS instruments have been tested for use in clinical research, clinical care, and validated in both genders as part of the PROMIS project.

**PROMIS Fatigue**

The PROMIS fatigue definition is “an overwhelming, debilitating, and sustained sense of exhaustion that decreases one's ability to carry out daily activities, including the ability to work effectively and to function at one's usual level in family or social roles” (Cella, et al., 2007). A higher score equals worse function or more symptoms, and individual items have been pulled from legacy instruments.

**PROMIS Sleep Disturbance**
The PROMIS sleep definition is “a rapidly reversible, current state of reduced (but not absent) awareness of and interaction with the environment” (Cella, et al., 2007). A higher score equals worse function or more symptoms; it provides a general measure of sleep disturbance. It has an unclear responsiveness to change in sleep pattern over time. Individual items have been pulled from legacy instruments.

**Self-esteem and Relationship (SEAR)**

The Self-esteem and Relationship questionnaire was developed to specifically address psychosocial issues related to erectile dysfunction (Althof, et al., 2003). It was designed as a measure for the emotional toll that erectile function can have on men, and detect meaningful clinical changes over time (Cappelleri et al., 2004). Some questions are reverse scored, and a higher score signifies a more favorable response for all 14 items.

**Short Form 12 (SF-12)**

The SF-12 was originally developed in 1996 (Ware, 1996), rooted in psychometric instruments used since the 1970s. While there is a complicated scoring algorithm, higher scores equal better health; its summary scores are very similar to those seen on the SF-36 (Jenkison & Layte, 1997).