# Definition and epidemiology of chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS)

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## Abstract

Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is a complex of symptoms including urological pain, with or without voiding symptoms. The symptoms resemble those of a prostate infection, but an infectious etiology is found in only 5–10% of cases. The prevalence is relatively similar across continents raising the possibility that the cause is not dependent on environment. The quality of life in men with CP/CPPS is worse than for some chronic medical diseases such as heart failure and diabetes mellitus. There is also an association with other chronic pain conditions, including irritable bowel syndrome (IBS), fibromyalgia (FM) and chronic fatigue syndrome (CFS). Other common symptoms in men with CP/CPPS are anxiety, depression and sexual dysfunction. Three quarters of men in a large American cohort study have symptoms attributable to the bladder. Men with CP/CPPS also commonly have sensitivity to some foods.

## Summary of recommendations

- Men with chronic pelvic pain should be assessed for pain referable to the bladder as this can help guide treatment.
- They should also be assessed for other overlapping chronic pain conditions including Irritable Bowel Syndrome, Fibromyalgia and Chronic Fatigue Syndrome.
- Other symptoms that should be inventoried are problems with anxiety, depression and sexual function including erectile dysfunction and premature ejaculation.

## 1 Definition/Classification of chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS)

Chronic pelvic pain syndrome is a symptom complex of urological pain complaints, with or without voiding symptoms. The distinguishing feature is pain, and separates a diagnosis of CP/CPPS from a diagnosis of lower urinary tract symptoms (LUTS) or benign prostatic hyperplasia (BPH). The term chronic pelvic pain syndrome (CPPS) is also called category III prostatitis, as set forth by a 1995 consensus conference, with the NIH (National Institutes of Health) classification published in 1999 [1]. The entire NIH classification is as follows:

- I. Acute prostatitis
- II. Chronic bacterial prostatitis
- IIIA. Chronic prostatitis/pelvic pain syndrome, inflammatory
- IIIB. Chronic prostatitis/pelvic pain syndrome, non-inflammatory
- IV. Asymptomatic inflammatory prostatitis

In 5 to 10% of cases, prostatitis is shown to have a bacterial etiology. The term prostatitis for category III may be confusing. Historically, the pain was thought to come from the prostate, from infection or inflammation. However, we now recognize that the prostate may not be the source of the pelvic pain in these men, and the term chronic pelvic pain syndrome was adopted to reflect this understanding. Category III is still subdivided as category IIIA, inflammatory, with the presence of white blood cells in EPS, VB3 or seminal plasma, or IIIB, non-inflammatory, without the inflammatory cells. To date, there have been no clinically significant differences demonstrated between these two subclasses.

The NIH definition as adopted by the Chronic Prostatitis Research Network is that of symptoms of pain or discomfort in the pelvis for at 3 of the previous 6 months [2]. Several exclusion criteria are also included, such as demonstration of uropathogenic bacteria detected by standard microbiological methods,



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urogenital cancer, prior radiation or chemotherapy, urethral stricture, or neurologic disease affecting the bladder [2]. Similar inclusion and exclusion criteria are being used in the ongoing NIH study on the Multidisciplinary Approach to Pelvic Pain (MAPP) [3].

Another term used is that of prostate pain syndrome, using the axial structure of the International Association for the Study of Pain (IASP) classification. The updated EAU (European Association of Urology) guidelines on pelvic pain [4] outlines this system of axes to further specify the location of the pain syndrome, under the umbrella term of chronic pelvic pain under Axis I, divided into disease if one is known as a cause of the pain, or as a syndrome when there is no proven infection or other obvious local pathology that may account for the pain. Axis II is the system, such as urologic, gastroenterological, peripheral nerves, psychological, etc. Axis III is the specific system, such as bladder or prostate. Other axes refer to symptom characteristics. A 2017 report by the International Continence Society has outlined the terminology and taxonomy of chronic pelvic pain syndromes [5].

# 2 Epidemiology

## *2.1 Incidence*

One study evaluated the incidence of CP/CPPS in a managed care population [ 6]. The incidence was 3.30 cases per 1,000 men per year, representing an incidence of 267,000 cases per year if these data can be extrapolated to the overall US population. In the Health Professionals Follow-up study, the incidence of new cases over 22 years was 3.3% [7].

## *2.2 Prevalence*

A recent review for the International Consultation on Urologic Disease (ICUD) sponsored by the Societé Internationale d'Urologie [8] indicated that prevalence of prostatitis-like symptoms ranged from 2.2% to 16%, with a median prevalence rate approximating 7.1% for chronic prostatitis/chronic pelvic pain syndrome. The mean prevalence in studies according to continent of origin ranged from 6.9% in North America to 12.2% in Africa, with Europe at 8.6%, 7.5% in Asia, and 7.6% in Australia. The relatively consistent rate across continents has suggested that it may develop independent of environmental factors specific to a given society. The Urologic Disease in America study reported an annualized visit rate of 1,798/100,000 population for prostatitis [9]. Thus, CP/CPPS is likely responsible for nearly two million physician visits annually in the United States alone.

There are no specific studies of older men but there are studies looking at the epidemiology of CP/CPPS in younger men. A study in 20-year-old Korean men reported a prevalence of 6% [10]. Studies of Canadian and African men age 16–19 years old reported prevalences of 8.3 and 13.3% respectively [11], [12]. Several factors were found to influence the prevalence and severity and QOL of young men in these groups. The Korean study found that in the multivariate model used, the likelihood of chronic prostatitis-like symptoms varied by the final educational level, with middle school and high school graduates having 1.8 and 1.4-fold higher odds, respectively, than men attending college. In the same model, the average duration of sunlight was also an independent risk factor of chronic prostatitis-like symptoms (odds ratio 0.85; 95% confidence interval 0.77 to 0.95; P=0.003). In African males, greater pain, urinary and depressive symptoms and rural setting of school were associated with diminished quality of life. In the young Canadian men, pain, urinary symptoms, depression and catastrophizing were correlated with diminished quality of life.

## *2.3 Demographics*

In the NIH-sponsored Chronic Prostatitis Collaborative Research Network (CPCRN) cohort study the mean age of participants was 42.8 years [2], similar to the current MAPP study [ 13], with an age range of 20–83. In the CPCRN cohort, the majority were white, educated beyond high school, currently employed, living with a partner and earning more than US $50,000 yearly. This was not a population-based study, so it is not clear that these characteristics are applicable to patients with CPPS as a whole.

## *2.4 Quality of life*

Men with CPPS report impairment in mental and physical domains of quality of life that is worse than

those reported for patients with congestive heart failure and diabetes [13], [14].

## 2.5 Association with other diseases

In an attempt to understand whether CPPS is a symptom of a systemic disease, studies have looked at what other chronic conditions are preset in men with CP/CPPS. In the CPCRN study that compared cases to age matched controls, men with CP/CPPS were 6 times more likely to self-report a history of cardiovascular disease, the most common being hypertension. An interesting follow-up study by Shoskes and colleagues found greater arterial stiffness in men with CPPS compared to controls [15]. This could represent evidence of greater sympathetic tone or a primary cardiovascular problem in these men. Assessment of arterial tone in these patients may become important to distinguish a cardiovascular phenotype. The association of hypertension and CP/CPPS was also examined in the Health Professionals Follow-up Study. This is a prospectively kept database of male health professionals. Using a definition for CP/CPPS of NIH-CPSI (National Institutes of Health Chronic Prostatitis Symptom Index) pain subscale scores >8, there was no association on multivariate analysis with hypertension overall, but there was in men with a BPH/LUTS history (OR 1.36). There was no association with overall or abdominal obesity, or for cigarette smoking [7]. Other studies have been mixed, reporting no correlation for hypertension as part of metabolic syndrome in men with CP/CPPS [16] or a significantly higher rate of hypertension in men with CP/CPPS than controls [17].

Men with CP/CPPS were 5 times more likely to self-report a history of nervous system disease compared to asymptomatic age matched controls in the chronic prostatitis collaborative research network (CPCRN) study [18]. In the NIH cohort, the symptom that most contributed to the difference in neurologic disease was numbness and tingling in the limbs. Although migraine headaches were common in the cases, they were not significantly different than controls. Also significant was a history of vertebral disc disease/surgery. Thus, subclinical disc disease or injury could be contributing to pelvic pain.

Another significant association is with other chronic pain conditions, irritable bowel syndrome (IBS), fibromyalgia (FM) or chronic fatigue syndrome (CFS). Although more common in females with chronic urologic pain, other conditions such as irritable bowel syndrome (IBS), fibromyalgia (FM) and chronic fatigue syndrome (CFS) may also contribute to the symptoms in men with CPPS [19]. In the ongoing NIH sponsored Multidisciplinary Approach to Pelvic Pain (MAPP) study, 31% of men with pelvic pain enrolled have one or more of these so called non-urologic associated somatic syndromes (NUAS), the most common being IBS; patients with NUAS also report more severe urological symptoms and more frequent depression and anxiety compared to those without NUAS [20].

## 2.6 Anxiety and depression

In the original CPCRN cohort study, men with CP/CPPS were twice as likely to report anxiety and depression as age matched controls [18]. Similar findings were reported in the subsequent MAPP study, as compared to age and education matched controls, males with pelvic pain showed greater levels of current and lifetime stress, poor illness coping and increased self-report of cognitive deficits. They did not self-report as high levels of childhood adversity as the females in the MAPP cohort [21]. A large database study from Taiwan found that men with CP/CPPS were significantly more likely to have a diagnosis of anxiety disorder than men without the diagnosis. The OR was 2.10 (95% CI=1.92, 2.29, p=0.001). The association held for all age groups, and was particularly strong in men aged 40–59 years old in which the OR was 2.53 [17].

## 2.7 Sexual dysfunction

We have come to recognize the significant prevalence of sexual dysfunction in even young men with CPPS [22]. The prevalence of ED (erectile dysfunction) in men with CP/CPPS is reported at 15–40% [ 23] In addition, a case control study of a large Taiwanese health database showed that men with a diagnosis of ED were more likely to have been previously diagnosed with CP/CPPS, 8.6%, compared to 2.5% of randomly selected controls (p<0.001) [24]. Other symptoms of sexual dysfunction are ejaculatory dysfunction/pain and premature ejaculation. From the CPCRN cohort, 74% of the men had ejaculatory pain at some point [25]. Similar levels of premature ejaculation have been reported [ 23]. These associations demonstrate the need for the assessment of sexual dysfunction in men with CP/CPPS, but also raise questions about what common mechanisms may be present in both conditions.

## *2.8 Epidemiology and clustering of symptoms*

The phenotype of patients meeting the criteria for CPPS is variable and can include several different types of symptoms. This has been well outlined by Shoskes and colleagues in the UPOINT classification [26]. This includes the categories of urinary, psychosocial, organ-specific, infection, neurologic/systemic and tenderness of skeletal muscle. More recently, the UPOINT system has been used to look at clustering of symptoms, to try to discern a common etiology for some groups of patients. A recent cluster analysis of men with CP/CPPS using the UPOINT system demonstrated two clusters: a “pelvic” group with the domains of urinary, organ specific and tenderness, and a “systemic group” of neurologic, infection and psychosocial [27]. It has been difficult in the past to apply the idea of separating patients with pelvic pain into subtypes, but these results suggest that this may be possible. The implications are significant for both investigation in to the pathophysiology, and also for selection of groups for clinical trials.

The NIH (U.S.) sponsored Multidisciplinary Approach to Pelvic Pain (MAPP) study has provided insights in to other aspects of the epidemiology of men with chronic pelvic pain who can be classified as CP/CPPS. Of 191 men enrolled in the first MAPP study, 75% were found to have either pain urgency, i.e. urgency to urinate due to pain pressure or discomfort and not due to fear of leaking, or pain that was made worse with bladder filling [28]. These symptoms are usually thought to be associated with interstitial cystitis/bladder pain syndrome (IC/BPS) [28] [29]. Compared to men with pelvic pain only, men with painful urgency or bladder pain had more flares, higher levels of catastrophizing and more frequently reported having irritable bowel syndrome. In the RAND Interstitial Cystitis Epidemiology male study, there was 17% overlap between men who met the high specificity IC/BPS definition and the case definition for CP/CPPS [30]. Thus, there is considerable symptom overlap between CP/CPP and IC/BPS as currently defined. This has led to the use of the term urologic chronic pelvic pain syndrome (UCPPS) to encompass both symptom based diagnoses.

## *2.9 Effect of lifestyle changes: diet and exercise*

In a survey of 62 patients with CPPS, 47% reported having sensitivity to some foods. The most common were spicy foods, coffee, tea, and chili [31]. There are no specific dietary recommendations for all patients with CP/CPPS and they should be individualized based on the patient’s food sensitivities. In a cohort study of men in Shanghai [32], multivariate analysis indicate that alcohol consumption, less water intake and a diet that favored meat or vegetables over the other increased the risk of symptoms of CP/CPPS. A study in men with CPPS demonstrated significant improvement in pain scores, quality of life and overall NIH-CPSI scores in men in an aerobic exercise group compared to placebo/stretching [33]. Other studies from China [32] and also a large cohort in the Health Professionals Follow-up study [ 34] have also confirmed the beneficial effects of exercise on the prevalence of symptoms of CP/CPPS.

# 3 Future research

Studies that can determine the age distribution in the population would be helpful. There are some discrepancies in the literature regarding what other systemic medical problems are associated with CP/CPPS, specifically hypertension. This may be an important point as this association could give insight into the as yet undetermined etiology of this condition. Further research to characterize the neurologic problems in these men is also warranted.

# 4 Conclusions

CP/CPPS was historically thought to be a chronic infection. More recent data has shown that not only are ongoing infections unusual in these patients, there are other medical problems and chronic overlapping pain conditions that suggest a more systemic problem. The relatively equal prevalence throughout the world is an intriguing finding and suggests that the etiology does not have to do with environmental factors. These patients have many other symptoms and problems besides just pelvic pain and need to be thoroughly evaluated to provide the best care.

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