

# A Bibliometric Analysis of Urologic Chronic Pelvic Pain Syndrome From 2000 to 2022

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**Purpose:** Urologic chronic pelvic pain syndrome has attracted a lot of attention in the new century, and an increasing number of relevant studies have been published. Therefore, we performed a bibliometric analysis of these publications, hoping to show the current research hotspots and future research trends.

**Methods:** The articles on were selected from the Web of Science Core Collection. Countries, authors, references and keywords in the field were visualized and analyzed using CiteSpace and VOSViewer software.

**Results:** A total of 1014 articles on urologic chronic pelvic pain syndrome were identified, with “chronic pelvic pain syndrome” being the most common keyword, with a strong association with “interstitial cystitis” and “chronic prostatitis”. The hotspot of urologic chronic pelvic pain syndrome research has gradually shifted from chronic prostatitis / urologic chronic pelvic pain syndrome to cystitis/bladder pain syndrome over the past few years. Future research tends to focus on urologic chronic pelvic pain syndrome etiology, including oxidative stress and inflammation.

**Conclusion:** Research on urologic chronic pelvic pain syndrome is steadily growing. The United States has made the most prominent contribution in this area, and the share of China's contribution is expected to grow further. The etiology of urologic chronic pelvic pain syndrome, including inflammation and oxidative stress, have been the focus of current research and developmental trends in the future research.

**Keywords:** bibliometric analysis, chronic pelvic pain syndrome, interstitial cystitis, chronic prostatitis, mechanisms, treatments

## Introduction

Pain is a suffering experience of sensory, emotional, cognitive and social components related to tissue damage or potential tissue damage. To encourage doctors to listen to their patients and assess their suffering, pain has been called the fifth vital sign since 1996.<sup>1</sup> Accordingly, in the past 20 years, people have paid more and more attention to urologic chronic pelvic pain syndrome (UCPPS), which encompasses two highly prevalent urologic chronic disorders—interstitial cystitis/bladder pain syndrome (IC/BPS) and chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS).<sup>2</sup> Because UCPPS is a heterogeneous disease both in presentation and pathophysiology, making characterization and reliable biomarker identification challenging,<sup>3</sup> the diagnosis of UCPPS mainly depends on the symptoms dictated by patients currently, which mainly including chronic pain of pelvis, urogenital tract floor or external genitalia, generally accompanied by lower urinary tract symptoms.<sup>4</sup> Studies have shown that UCPPS has a serious negative impact on patient quality of life, and patients with UCPPS may have a worse quality of life than those with end-stage renal disease.<sup>5</sup> The prevalence of UCPPS has shown an increasing trend over the years, with community-based surveys reporting a prevalence of 8% in men, but estimates are that it can be as high as 11.5% in men under 50 years of age,<sup>5</sup> and up to 7% of women were affected by IC/BPS.<sup>6,7</sup> Although researchers have done a lot of basic and clinical exploration, the cause and effective treatment of UCPPS are still inconclusive.

Bibliometrics is a discipline that describes and analyzes the research trends and progress in a certain field, which began in 1969. It takes scientific literature as the research object, and quantitatively studies the characteristics and relationship between scientists and scientific literature by using statistical analysis, social network analysis and mathematical modeling.<sup>8</sup> At the same time, visual co-citation analysis can explain the data more conveniently, show the data more comprehensively, and help to mine the internal relations among the data.<sup>9</sup> Software is critical to scientific research: it helps scientists identify research questions, analyze data, visualize results, and disseminate knowledge. We have chosen Citespace and VOSviewer as our analysis tools in this research. Citespace pays attention to the strength of the relationship in terms of graphics and connections, while VOSviewer mainly constructs the relationship by distance.<sup>10</sup> The two software have their own advantages and can play a complementary role.

This study aims to show the development status and structure, development frontier and evolution path of UCPPS in the form of knowledge mapping, and on this basis, selects the core literature in the field for reading, analysis and review, so as to provide new ideas for UCPPS study.

## Materials and Methods

### Data Collection

In order to collect comprehensive and authoritative articles, we chose Web of Science Core Collection as the data source. The search formula was set to TS = (“Urologic chronic pelvic pain syndrome” OR (“chronic pelvic pain” AND (“prostatitis” OR “Cystitis”))), and the timespan of the search were from January 1, 2000, to August 1, 2022. With limiting the type of literatures to be ‘Articles’, we retrieved 1084 articles. Then we excluded proceeding papers and early accesses, and finally got 1014 papers. ALL of these papers are exported as TXT files in the form of all records and references. The complete data acquisition process is illustrated in Figure 1.

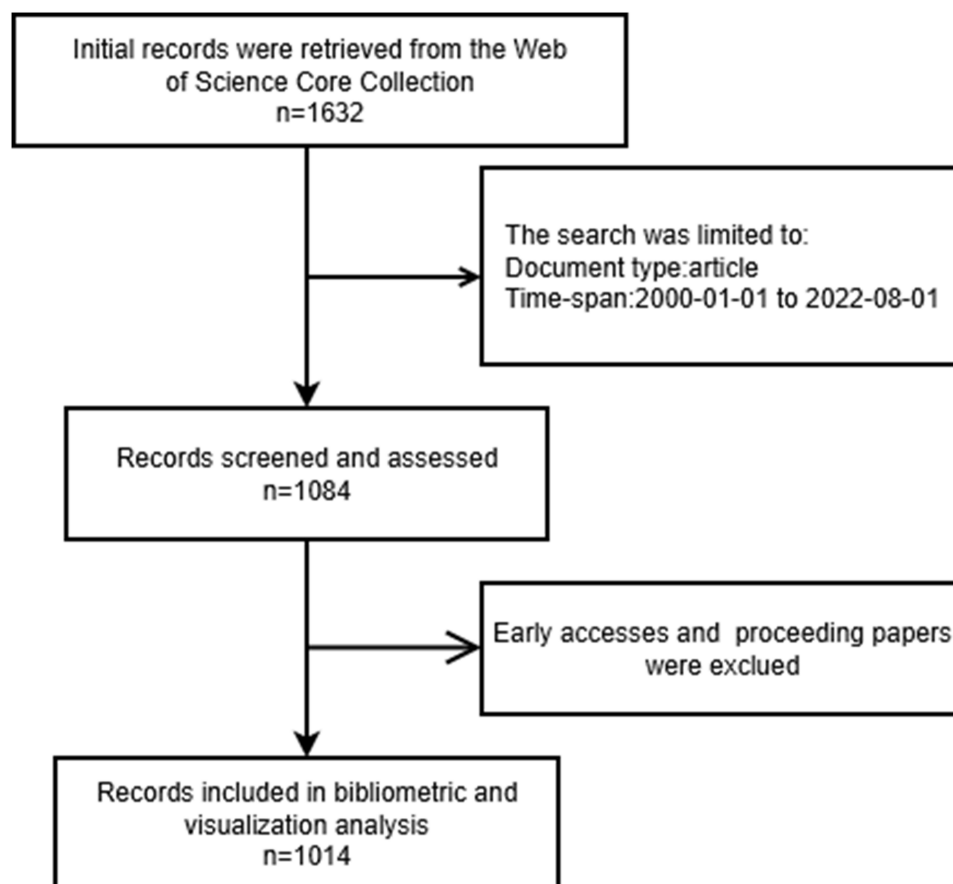


Figure 1 Flow chart for publications selection.

## Data Analysis

All the data we collected in Web of Science Core Collection were imported into the Microsoft Excel 2019, Citespace and VOSviewer for visual analysis.

With the technical progress in the field of knowledge mapping, the existing information visualization techniques make knowledge mapping have the function of supporting multivariable, time-sharing and dynamic complex network analysis. Citespace and VOSviewer, as representative tools, are widely used to study the trends and evolvments of different disciplines.<sup>9,11</sup> CiteSpace is based on the data normalization method of set theory for similarity measurement of knowledge units, and the similarity algorithm is used to obtain timezone and timeline within time slices, so that the process of knowledge evolution and the historical span of literature in a certain cluster can be clearly outlined in the time dimension to understand the development process and trend of the field.<sup>9,12</sup> Vosviewer uses a probabilistic data normalization approach, providing various visualization views in the fields of keywords, co-authorship, co-organization, and co-authorship, including Network Visualization, Overlay, Visualization, and Density Visualization.<sup>11</sup> In the form of display, We use Microsoft Excel 2019 to analyze annual publication trends, and CiteSpace and VosViewer software to analyze country and institutional distribution, author contributions, core journals, keyword and timezone viewer. These bibliometric studies based on scientific papers and citation data explore and predict the development characteristics and evolution law of UCPPS researches from different dimensions and perspectives.

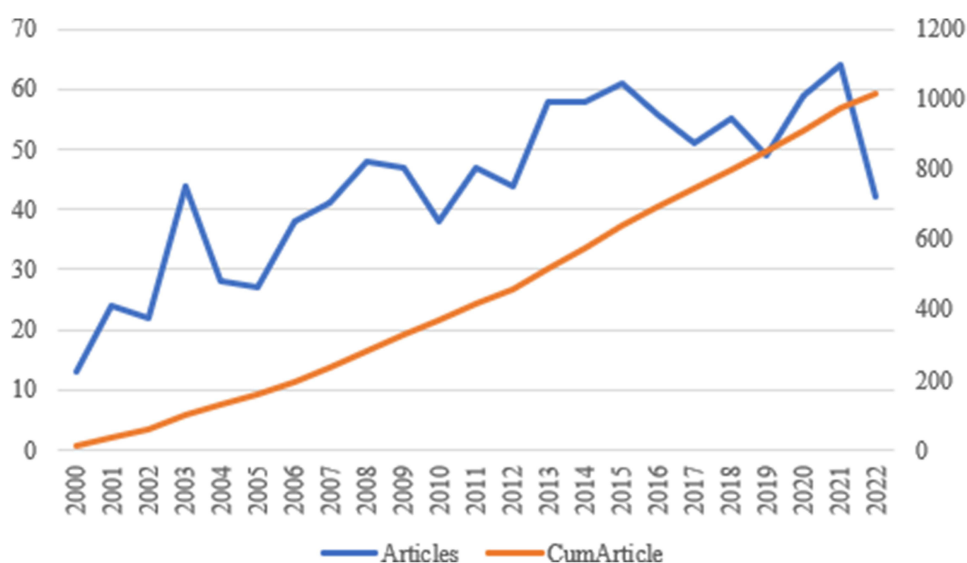
## Results

### The Trend of Publication Outputs

The number of publication outputs show the development trend in the research field. From January 2000 to August 2022, we searched 1014 valid literatures from Web of Science Core Collection. The 1014 papers used in this study were from 3086 authors at 1139 organizations in 52 countries and regions, published in 244 journals, and cited 11,793 citations from 3904 journals. We import the data collected from Web of Science Core Collection into Excel to get Figure 2, from which we can see that UCPPS has maintained a certain popularity in the past 20 years, especially after 2013, the number of articles has been kept at 50 per year, which indicates that UCPPS field has recently received more attention from researchers and become a new hot spot in the intersection of urology and pain disciplines.

### The Analysis of Distribution and Collaboration Relationship of Countries/Regions

The address information of the authors of the article contains the institution where each author is located and its corresponding country, which can be used to analyze the geographical distribution of the authors of the paper. It can be



**Figure 2** Trends of UCPPS publications over the past 22 years.

seen from Figure 3 that developed countries such as Europe and the United States occupy a dominant position in the production of UCPPS research papers. Among them, the United States, as the first country that began to pay attention to this field, has the largest number of related papers, accounting for nearly 50% of the total, that is, about one-second of UCPPS papers contain at least one American author, indicating that the United States produces knowledge on this topic. Contribute the most. China followed closely, ranking second, with a cumulative output of more than 147 papers, accounting for 14.5% of the world's total. The third place for the number of papers is Canada, with a total of about 93 papers (7.8%). Followed by developed countries in Europe and East Asia such as Italy, Germany, the United Kingdom, South Korea and Japan. It is worth noting that Turkey, a Middle East country, also has a relatively bright performance in UCPPS research, with more than 30 papers, accounting for about 3.1%.

The development of communication technology and the process of economic globalization have promoted the increasing internationalization of scientific research. In the global UCPPS research, the cooperation between countries is becoming more and more frequent, and the proportion of international cooperative papers is increasing year by year. Figure 4 shows the partnership and the intensity of cooperation between the individual countries, "total link strength" represents the number of papers produced by inter-country collaboration. From the perspective of "total link strength", the United States is the core force in the current international cooperation network of UCPPS, which had the strongest collaboration with Canada. But in terms of centrality (Table 1), Germany tops the list. Although its publication outputs are not so much, it occupies an important position in the cooperation network and has a high degree of cooperation. In addition, Canada, England, Australia, Egypt, Argentina, China, and Italy also have many cooperative relationships. Among them, although China has the second most outputs and a large number of international cooperation papers, it ranks lower in the closeness centrality indicators, indicating that China's cooperation objects are relatively fixed and the scope of cooperation is limited.

## The Analysis of Authors and Co-Authorship

The core author is not only the backbone of academic innovation and discipline development, but also one of the important factors to enhance the academic influence and competitiveness of journals. Price studied the relationship between the number of scientists and the number of scientific literatures, and noticed the great role of elites in the development of science, as well as the quantitative relationship between scientists at different levels of ability, and put forward "Price's Law" in 1963, that is, half of the papers on the same topic were written by a group of high-productivity authors, and this set of authors was equal to about the square root of the total number of authors. According to Price's Law, the minimum number of papers published by core authors in a certain field is  $m = 0.749 \times n_{\max}^{1/2}$ , where  $n_{\max}$  represents the number of papers published by the most prolific authors in the field. In this study, the author with the

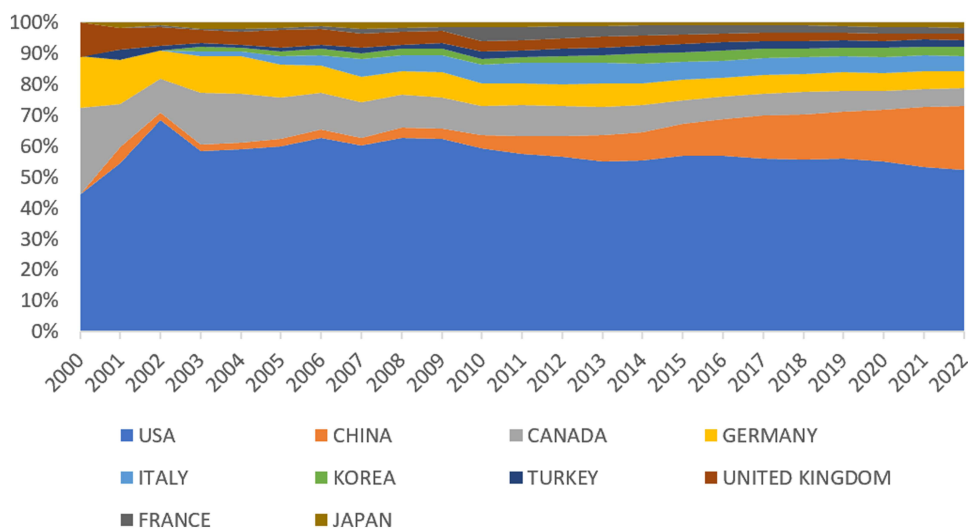
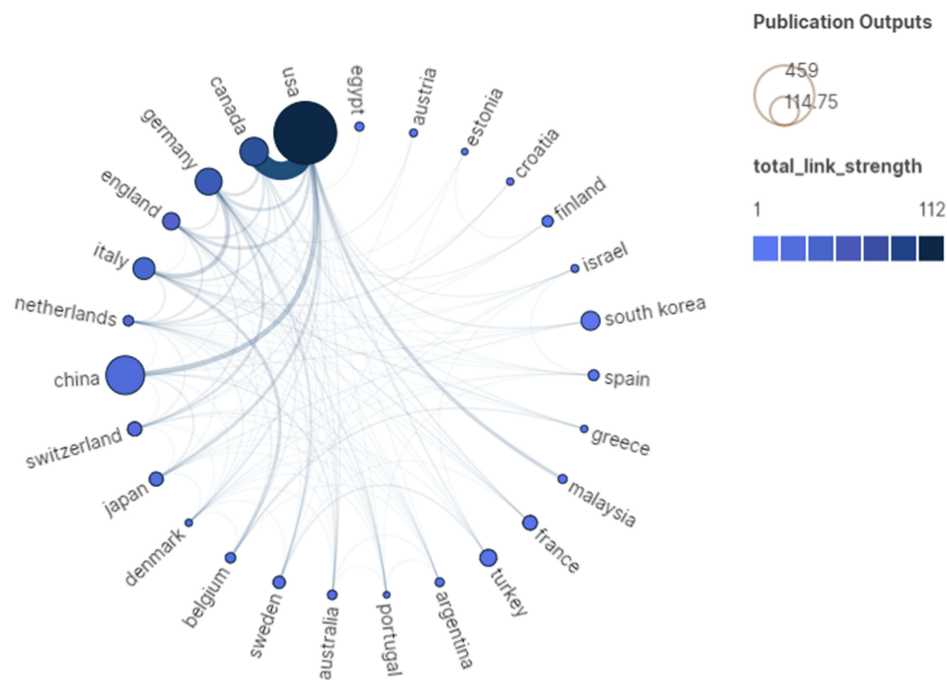


Figure 3 The top 10 most active countries/regions.



**Figure 4** The co-authorship map of countries. The thickness of the connecting lines shows the frequency of cooperation, “total link strength” represents the number of papers produced by inter-country collaboration.

highest number of publications was NICKEL JC, with a total of 76 publications. After calculations, we get  $m \approx 6.5$ , so we conclude that authors with more than 7 papers published are defined as the core authors in the UCPPS field.

What Price’s law reveals is that the so-called “core” authors are found from the perspective of the volume of publications. However, the importance and influence of an author can be measured only by the volume of his or her output, which is somewhat one-sided. In 2005, Jorge Hirsch proposed h-index to measure core scientists, which point out that the h-index of a scholar is the number of papers that have been cited at least h times.<sup>13</sup> It can reflect the influence of a scientist’s academic papers and also the number of important papers he or she has produced. But h-index is insensitive to highly cited articles. Subsequently, the g-index is proposed as an improvement of the h-index, shows that when a set of articles ranked in descending order of their citations, the g-index is the order of the largest paper with at least  $g^2$  cumulative citations  $g$ .<sup>14</sup> We use h-index, g-index, total number of citations (TC), number of publications (NP), to evaluate the influence of relevant authors (Table 2).

**Table I** Centrality of Inter-Country Cooperation

Country	NP	Centrality	Total-Link-Strength
Germany	83	0.34	59
USA	459	0.24	112
Canada	93	0.18	76
England	32	0.12	39
Netherlands	12	0.09	34
Australia	10	0.07	16
Egypt	9	0.06	1
Argentina	9	0.06	11
China	145	0.06	27
Italy	55	0.05	37

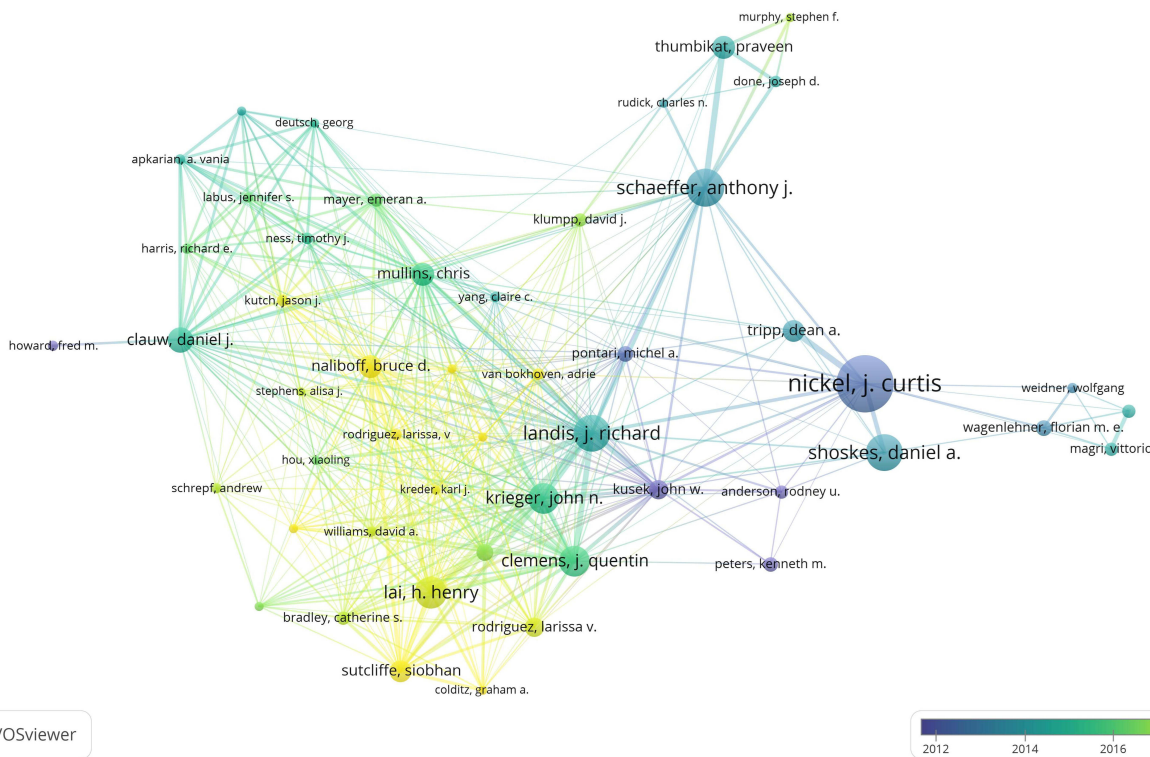
**Table 2** Top 10 Authors Related to UCPPS

Name	h-Index	g-Index	TC	NP
Nickel JC	41	64	4191	76
Landis JR	30	44	2275	44
Shoskes DA	28	42	2097	42
Schaeffer AJ	27	44	2306	44
Kusek JW	21	25	1717	25
Krieger JN	20	36	1403	36
Clemens JQ	18	32	1226	32
Mullins C	18	21	832	21
Pontari MA	18	23	1339	23
Clauw DJ	17	22	927	22

Co-authorship map reflects the collaborative relationships of research teams in the field, we visualize the cooperation network for core authors by VOSviewer. At the same time, we added a time dimension to show the passage of time through the gradual change of color. The analysis results are shown in Figure 5. In Figure 5, the node size represents the number of papers published, the node color represents the time distribution, and the line represents the partnership. As can be seen from the picture, the co-occurrence network of high-productivity authors in UCPPS is an overall network graph with high connectivity, which means that there is a wide range of cooperation among these authors, a high degree of cooperation between different teams.

### The Analysis of Relevant Journals

The development of science always follows certain laws. On the one hand, modern science and technology intersect and interpenetrate each other. On the other hand, there is a tendency for small subjects to be integrated into large subjects.



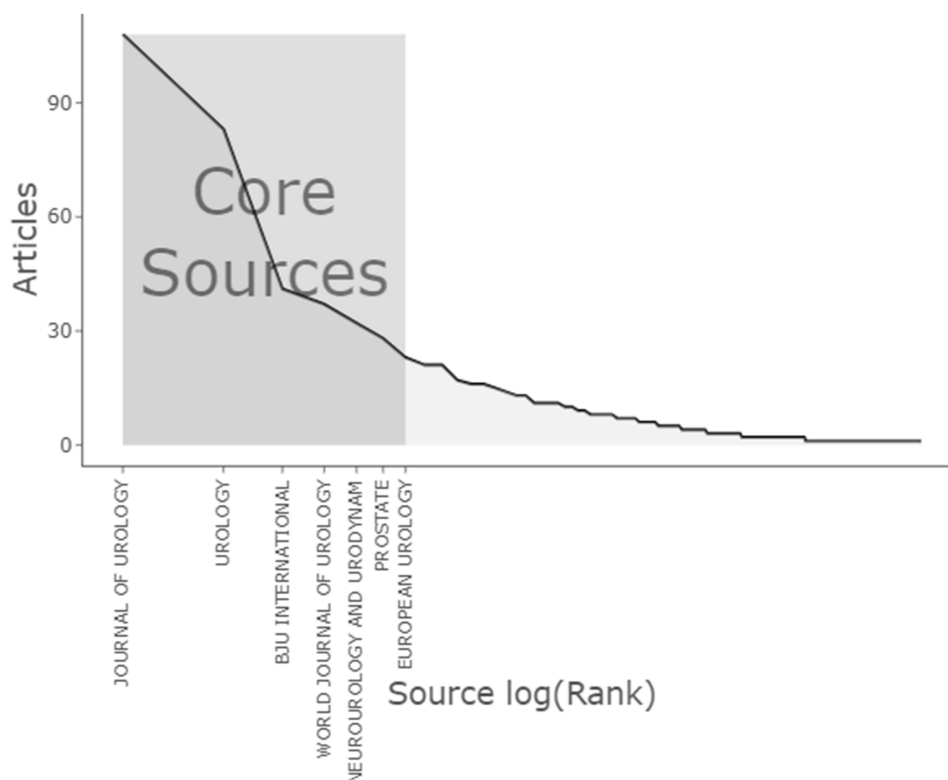
**Figure 5** The co-authorship map of authors related to UCPPS. The size of the nodes indicates the number of documents published by the author in collaboration, and the thickness of the edges indicates the frequency of collaboration; the gradual change of color shows the passage of time.

Bradford summed up the law of dispersion of literature starting from the law of scientific unity. Bradford pointed out that if scientific journals are arranged in decreasing order according to the number of papers published in a certain discipline, then the journals can be divided into a core area dedicated to this discipline and several areas containing the same number of papers as the core area.<sup>15</sup> In Figure 6, according to Bradford's Law, the 244 document sources were divided into three zones, zone 1 had 7 journals, zone 2 had 32, and zone 3 had 205. The journals in the zone 1 (core area) include *Journal of Urology*, *Urology*, *BJU International*, *World Journal of Urology*, *Neurourology and Urodynamics*, *Prostate* and *European Urology*. *Journal of Urology* ranked first with 108 publications, accounting for 10.6% of the total, and "Urology" ranked second with 83 publications.

Subsequently, we applied h-index, g-index, total number of citations, number of publications to evaluate the impact of relevant journals. As we can see from Table 3, *Journal of Urology* has the highest h-index, g-index, total number of articles published and total number of citations, and is deservedly the most influential journal in UCPPS. *International Urogynecology Journal*, *Journal of Sexual Medicine*, *Pain* appeared in the table, although they were not rated as core journals according to Bradford's Law. It is worth mentioning that *Pain* has an average number of citations per article of 23.6, which is even higher than *Prostate*.

## The Analysis of Co-Cited References

Co-citation network based on CiteSpace generated references of UCCPS papers. Each node in the graph represents a document, and the line between each node indicates the citation relationship between the documents; the automatic clustering labels use LLR algorithm. Cluster size in graph A indicates the number of citations, reflecting the degree of attention the clusters have received. The size of the nodes in the graph B reflects the centrality of the article, centrality depicts the node establishing a bridge between 2 unrelated nodes, with a high mediated centrality highlighting the importance of the node in the knowledge structure.



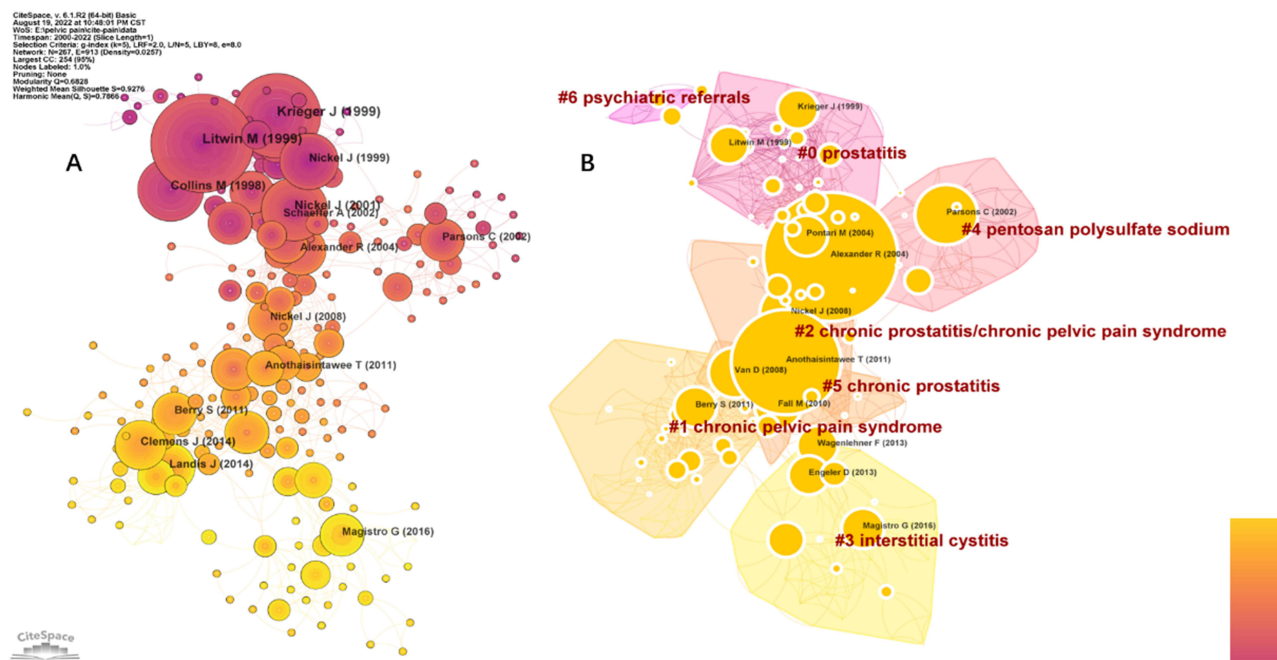
**Figure 6** Journals clustering through Bradford's law. According to Bradford's Law, the logarithm of the number of ranked journals (Source log(rank)) is the horizontal coordinate, and the corresponding number of papers (Articles) is the vertical coordinate.

**Table 3** Top 10 Journals Related to UCPPS

Element	h-Index	g-Index	TC	NP
Journal of Urology	45	64	4780	108
Urology	31	49	2699	83
Bju International	26	41	1756	41
World Journal of Urology	21	32	1074	37
European Urology	20	23	1485	23
Journal of Sexual Medicine	14	17	526	17
Prostate	13	21	462	28
International Urogynecology Journal	11	14	362	14
Neurourology and Urodynamics	11	17	332	32
Pain	11	15	354	15

Figure 7A and Table 4 show the high co-cited articles, Litwin M developed of a psychometric index of symptom and quality of life impact in men with chronic prostatitis,<sup>16</sup> The article by Krieger J refined the definition and classification of prostatitis,<sup>16</sup> Collins M explored the epidemiology of physician visits for genitourinary symptoms or a diagnosis of prostatitis.<sup>17</sup> The “Multidisciplinary Approach to Chronic Pelvic Pain Research” (MAPP) research network was established to better understand and treat UCPPS,<sup>18</sup> Magistro G evaluated the best available practical evidence recommendations and randomized controlled trials of CP/CPSP treatments and management.<sup>19</sup> These high co-citation articles build the knowledge base of UCPPS. Figure 7B shows the largest 7 clusters of co-cited references. From the point of time distribution, the research direction and contents of UCPPS has obvious stage characteristics: while the early researchers focused on chronic prostatitis, in recent years more attention has been paid to interstitial cystitis.

The dual-map overlay of journals demonstrated relationship distribution among journals, with citing journals on the left and cited journals on the right, and the colored paths between them suggesting the cited relationships.<sup>20</sup> The orange path in Figure 8 indicates that the documents published in Molecular/Biology/ Genetics journals are often cited by Molecular/Biology/ Immunology journals. Relevant citations reached 2460 times.



**Figure 7 (A)** The network of co-cited references. **(B)** The network of co-cited references clusters. Cluster size in graph **(A)** indicates the number of citations, reflecting the degree of attention the clusters have received. The size of the nodes in the graph **(B)** reflects the centrality of the article, centrality depicts the node establishing a bridge between 2 unrelated nodes, with a high mediated centrality highlighting the importance of the node in the knowledge structure.



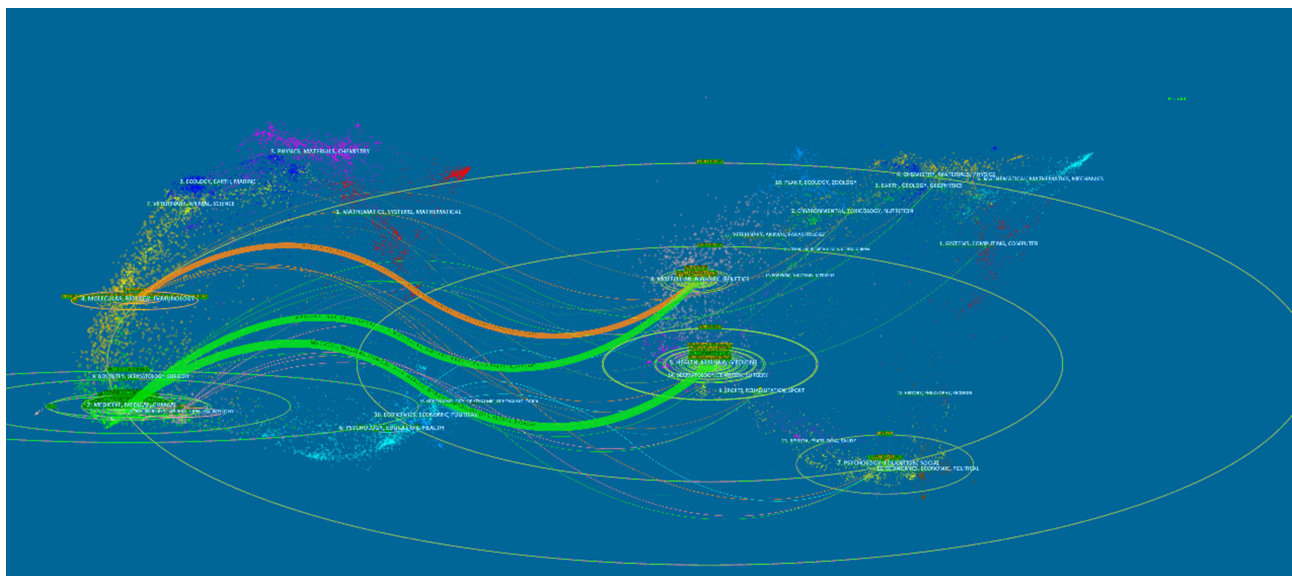
**Table 4** Top 10 Co-Cited References Related to UCPPS

Citation Counts	Author	DOI	Year
88	Litwin M	10.1016/S0022-5347(05)68562-X	1999
68	Krieger J	10.1001/jama.282.3.236	1999
52	Collins M	10.1016/S0022-5347(01)63564-X	1998
50	Nickel J	10.1016/S0022-5347(05)66541-X	2001
36	Landis J	10.1186/1471-2490-14-58	2014
36	Magistro G	10.1016/j.eururo.2015.08.061	2016
36	Nickel J	10.1016/S0090-4295(99)00205-8	1999
33	Alexander R	10.7326/0003-4819-141-8-200410190-00005	2004
30	Schaeffer A	10.1016/S0022-5347(05)64686-1	2002
29	Pontari M	10.1097/01.ju.0000136002.76898.04	2004

At the same time, the two green paths show that articles in Medicine/Medical/Clinical journals often cite articles in Molecular/Biology/Genetics and Health/Nursing/Medicine journals, with a frequency of 3406 and 5656 citations, respectively.

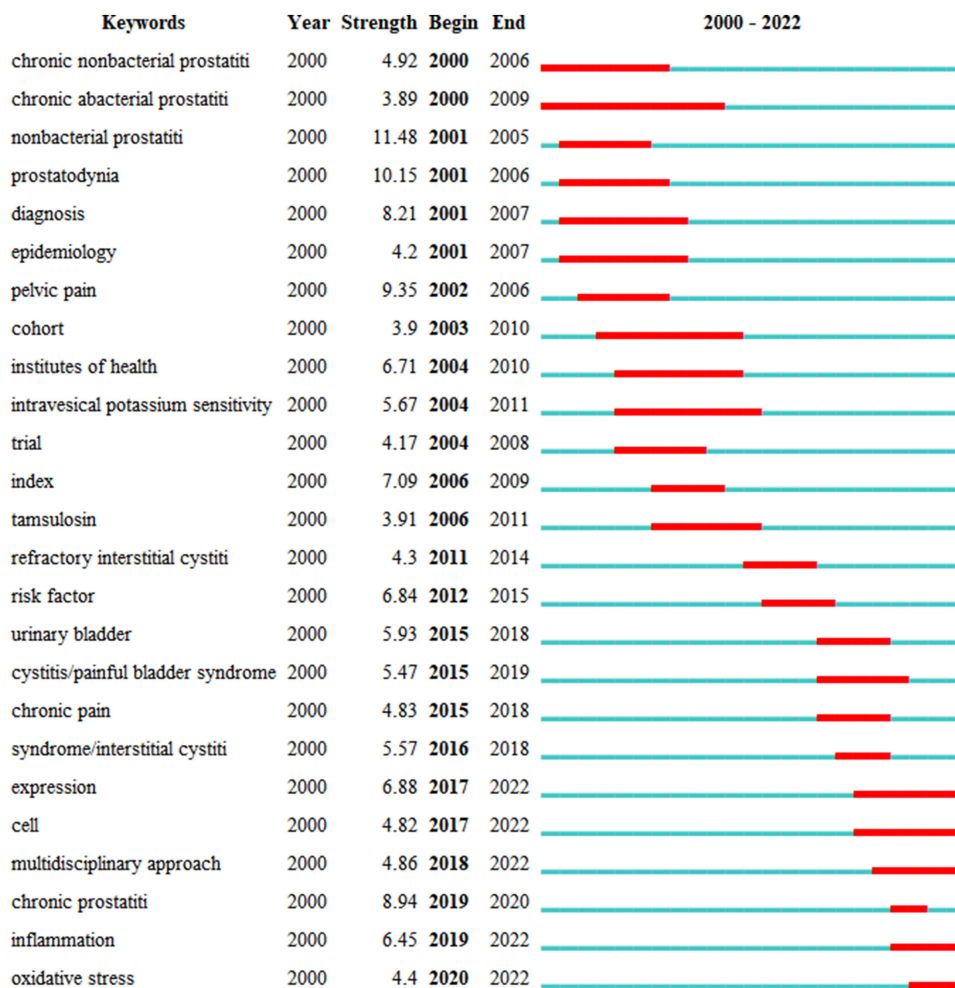
## The Analysis of Hotspots and Frontiers

The keywords condense the core and essence of a paper, and the keyword co-occurrence analysis can reveal the research hotspots in a scientific field. The keyword co-occurrence network view of 1014 literatures were drawn by VOSviewer, and 82 key keywords with frequency greater than or equal to 5 were selected for visualization (Figure 9). In Figure 9, the circle nodes represent keywords and the connecting lines represent co-occurrence relationship, the larger the circle node, the more frequent the keyword appears and the more representative of the domain hotspot. The thickness of the line represents the strength of the association, the thicker the line, the more often they appear together in the same paper; Node colors represent different clusters, for example, study topics. “Chronic pelvic pain syndrome” is the most common keyword, with a strong association with “interstitial cystitis” and “chronic prostatitis”. Excluding search terms, we can find that inflammation, sexual dysfunction, quality of life, endometriosis, questionnaires, treatment, diagnosis, irritable-bowel-syndrome, lower urinary tract symptoms, acupuncture, NIH-CPSI, vulvodynia are mentioned many times, which means that UCPPS is primarily concerned with its diagnosis, treatment, comorbidities, and impact on patients’ lives.



**Figure 8** The dual-map overlay of journals on UCPPS. The dual-map overlay of journals demonstrated relationship distribution among journals, with citing journals on the left and cited journals on the right, and the colored paths between them suggesting the cited relationships.





**Figure 10** Top 25 Keywords with the Strongest Citation Bursts. The blue line indicates the time interval, while the red line indicates the time period when a keyword had a burst.

## IC/BPS

### Possible Mechanisms of IC/BPS

IC/BPS is defined as chronic bladder-related pelvic pain, pressure or discomfort with other urinary symptoms, such as persistent urge to urinate or urinary frequency, that are not confused with the disease. The cause of IC/BPS is not yet clear and the following possible mechanisms have been proposed.

#### Autoimmunity/Inflammation

Histological analysis of bladder specimens from patients with IC often shows mast cell infiltration, high levels of pro-inflammatory cytokines and chemokines detectable in the serum, bulbous cystoscopic haemorrhages following hydro-dilation, and erosion and thinning of the bladder wall, all suggesting a role for inflammation in the pathogenesis of IC.

#### Infections

The high positive rate of urine cultures, alterations in urine bacterial flora or whole transcriptome analysis suggest that urinary tract infections are associated with IC/BPS. Recurrent female urinary tract infections can cause hypersensitivity symptoms in the female bladder through a variety of factors, such as induction of apoptosis in the urinary tract epithelium, increase in the number of mast cells, and decrease in epithelial calmodulin.<sup>23</sup>

### Neurological Factors

Histopathology shows characteristic nerve endings proliferation and chronic peripheral neuritis in the bladder wall.<sup>24</sup> The main neurological factors in patients with IC are: 1. increased sympathetic activity;<sup>25</sup> 2. upregulation of peripheral and central sensory innervation;<sup>26,27</sup> 3. increased nerve fibre density;<sup>28</sup> 4. neuroinflammation.<sup>29,30</sup>

### Muscle Dysfunction

Permeability damage or alterations to the GAG layer or uroepithelium, increased numbers of mast cells in the pushing muscle or altered NO levels and ATP/NO ratios in patients with IC can lead to pushing muscle dysfunction and cause IC-like symptoms.<sup>31</sup> The higher incidence of IC with a history of pelvic surgery and anal raphe pain suggests that pelvic floor muscle dysfunction may also contribute to the development of disease symptoms.<sup>32</sup>

### Psychological Factors

Patients with IC often present with psychiatric abnormalities that have a significant impact on psychosocial functioning and quality of life. Pain, sleep disturbances, depression, anxiety, stress, social dysfunction and sexual dysfunction are significantly more common in patients with IC/BPS than in non-IC patients,<sup>33</sup> and it has been suggested that IC/BPS may be part of a family of hypersensitivity disorders affecting the bladder and other somatic/invasive organs as part of a systemic disorder.<sup>34</sup>

### Other Factors

IC is often combined with fibromyalgia, irritable bowel syndrome, chronic fatigue syndrome, dry syndrome and chronic headache. The mechanisms are unclear and may be part of a systemic disease.<sup>35</sup> Components of the urine such as potassium ions may disrupt the uroepithelial function of the bladder causing symptoms, eg long-term abuse of ketamine producing IC-like symptoms may be related to the metabolites of the ketamine machine.<sup>36</sup> Patients with IC find a reduction in subannual microvascular density and cut hyperbaric oxygen therapy relieves the symptoms of IC, suggesting that tissue hypoxia may be an etiology of IC.<sup>37</sup> Consumption of specific foods or beverages is often a cause of exacerbation of IC symptoms, seen in 52.7–95.8% of patients, suggesting that there may be a broader range of factors in the etiology of IC that still need to be explored in further research.

### Current and Potentially Viable Treatments of IC/BPS

The main aim of treatments is to improve the patient's quality of life through controlling pain and reducing symptoms.

#### Conservative Treatments

Behavioral therapy and Psychotherapy are important in relieving patients' discomfort.

#### Medication

Several drugs such as dulcolytin, gabapentin, montelukast, NSAIDs, sildenafil, adalimumab, certolizumab and tacrolimus are described recently to alleviate the symptoms.

#### Surgical Treatments

Hydrodilatation and Transurethral ablation/electrocautery have often been reported of better results. However, the reduction in bladder volume is a concern and controversial.

Cystectomy and urinary diversion will be the last option. Long-term postoperative observation is required to monitor for symptom recurrence and complications such as hydronephrosis and adenocarcinoma of the bowel segment.

#### Physiotherapy

Biofeedback: reduces the resting tone of the pelvic floor muscles and works well in synergy with medication. Patients learn how to relax the pelvic floor muscles during pelvic pain, eliminating the "pain-muscle spasm-pain" cycle and improving symptoms.<sup>38</sup>

Acupuncture: Recent reports have shown that IC patients who have failed to pharmacological treatments, acupuncture may be an optional choice.<sup>39</sup>

### Neuromodulation

Neuromodulation is the fourth line of treatment for patients with bladder pain syndrome/interstitial cystitis (BPS/IC) after failure of behavioral and pharmacological treatments. Sacral neuromodulation may be effective in patients with BPS without Hunner's lesion and the effects appear to be maintained in the mid- and long-term. Selective pudendal nerve stimulation has a high response rate when pudendal neuralgia is suspected.<sup>40</sup>

### Self-Management

Patients can self-manage a certain amount of their symptoms by changing behaviors, which includes their diet, fluid management and stress management.<sup>41</sup> Corresponding timely and supportive information can effectively improve the effectiveness of patient self-management,<sup>42</sup> suggesting that clinical workers need to pay more attention to patient feedback.

## CP/CPPS

### Possible Mechanisms of CP/CPPS

Chronic prostatitis is one of the most common diseases among adult men. In 1995, the NIH defines Type III chronic prostatitis as CP/CPPS based on basic and clinical research on prostatitis, which accounting for approximately 90% of chronic prostatitis. The pathogenesis of CP/CPPS is not yet clear, it can be caused by the following factors.

### Pathogenic Infection

It may be associated with certain specific pathogens, such as anaerobic bacteria, L-type Aspergillus, nanobacteria or Chlamydia trachomatis, mycoplasma and other infections, and studies have shown that the local prokaryotic DNA detection rate in patients with this type is as high as 77%.<sup>43</sup>

### Urinary Dysfunction

Certain factors cause excessive contraction of the urethral sphincter, resulting in bladder outlet obstruction with residual urine formation, causing urine to flow back into the prostate, which can not only bring in pathogens but also directly irritate the prostate and induce sterile chemical prostatitis, leading to abnormal urination and pain in the pelvic region.

### Psychosomatic Factors

Some studies have shown that many of the mechanisms of CPPS are based on central nervous system associations. Men with depression and anxiety in the general population have higher prostatitis scores.<sup>44</sup> Psychopathological factors and personality -specific changes are evident in more than half of patients with persistent prostatitis.<sup>45</sup> These changes in mental and psycho-logical factors can cause autonomic dysfunction, resulting in posterior urethral neuromuscular dysfunction.<sup>46</sup>

### Neuroendocrine Factors

Patients with prostatitis may have alterations in the resting state neuro-muscular junction and these patients are often prone to fluctuations in heart rate and blood pressure, suggesting a possible association with autonomic responses.<sup>47</sup> Local stimulation of the prostate and urethra, through nerve impulses, promotes the release of norepinephrine, prostaglandins, calcitonin gene-related peptides, and substance P from sympathetic nerve endings,<sup>48</sup> causing vesicourethral dysfunction and leading to abnormal activity of the perineum and pelvic floor muscles, with persistent pain and involvement pain in the corresponding areas outside the prostate.<sup>49</sup>

### Abnormal Immune Response

Recent studies have shown that immune factors play an important role in the development of type III prostatitis. Changes

in the levels of certain cytokines, such as IL-2, IL-6, IL-8, IL-10, TNF- $\alpha$  and MCP-1, can occur in the prostatic fluid and seminal plasma and tissues and blood of patients.<sup>50–53</sup>

### Oxidative Stress

Under normal circumstances, oxygen free radicals are in a state of dynamic balance. In prostatitis, the excess production of oxygen free radicals and the relatively reduced role of the free radical scavenging system result in nerve endings supersensitive, which may also be part of the pathogenesis.

### Pelvic-Related Disease Factors

Patients with prostatitis often have dilated venous plexuses in the peripheral zone of the prostate, haemorrhoids and varicose veins of the spermatic cord, suggesting that some patients' symptoms may be related to pelvic venous congestion and blood stasis.

### Lower Urinary Tract Epithelial Dysfunction

Several studies have found many similarities between CPPS and IC, and it is hypothesized that the two share a similar pathogenesis. Lower urinary tract epithelial dysfunction is caused by a disruption in the balance between potentially protective and damaging factors in the lower urinary tract epithelium.

### Current and Potentially Viable Treatments of CP/CPPS

Not all patients with chronic prostatitis need treatments, the main point is to relieve pain, alleviate urinary symptoms and improve the quality of life.

### Healthy Lifestyle

Patients should maintain good lifestyle habits, including abstaining from alcohol, avoiding spicy and stimulating foods, avoiding holding urine, being sedentary, keeping warm, strengthening physical exercise, and having a regular sex life, which can help improve symptoms in patients with prostatitis.

### Medication

- (1) Oral antibiotics such as fluoroquinolones are recommended for 2–4 weeks, and then the decision to continue antibiotic therapy is all based on feedback on efficacy. It is only recommended to continue taking it for 4–6 weeks when the symptoms are reduced.
- (2)  $\alpha$ -blocker is a basic drug for the treatment of type III prostatitis and can be used in combination with antibiotics to improve lower urinary tract symptoms and pain by relaxing the smooth muscles of the prostate and bladder.
- (3) Saw Palmetto and Cernilton have previously been used successfully to improve the symptoms of CP/CPPS patients.<sup>54</sup> This may be due to the antioxidant properties of phytotherapy as both a free radical scavenger and a xanthine oxidase inhibitor.<sup>55,56</sup>
- (4) M-blockers for patients with prostatitis with manifestations of overactive bladder disorder such as urinary frequency and urgency and nocturia but without obstruction.
- (5) Antidepressants and anxiolytics for patients with chronic prostatitis who have a combination of depression, anxiety and other mood disorders, antidepressants and anxiolytics can be used as an alternative treatment along with prostatitis.
- (6) Chinese herbal medicine A randomized double-blind placebo-controlled study has shown that herbal medicines such as Ning Mi Tai Capsules are safe and effective in the treatment of type III prostate.<sup>57</sup>
- (7) Botulinum toxin A may represent a promising therapeutic strategy for these patients.<sup>58</sup> Botulinum toxin can inhibit the release of acetylcholine from nerve fiber endings, which determines a transient skeletal muscle relaxation and produces an analgesic effect by reducing muscle hyperactivity.<sup>59</sup>

The etiology of both diseases is not fully understood, but infection, immunity, inflammation, and psychosomatic factors are common influences in both. Pathogenic infection is a common factor, but there are significant differences in

the microbiota of them.<sup>60</sup> Research studies have demonstrated that symptoms of both are significantly worse during times of high mental stress.<sup>49,61</sup> When it comes to treatment, they share the same principles of symptom improvement, pain control and quality of life. Conservative treatment includes behavioral therapy as well as psychological guidance, pharmacological treatment is mainly antibiotics and allopathic medicines, and other treatments biofeedback, massage therapy and acupuncture also have commonalities. Both are clinical syndromes characterized by pelvic pain, and it is not meaningful to try to distinguish them completely based on current definitions. The questions that need to be addressed are how patients with only pelvic pain differ from those with co-existing urinary symptoms and, in addition, what are the differences in the nature of pelvic pain in men and women.<sup>62</sup>

## Conclusion

This study used a bibliometric approach to conduct a comprehensive analysis of studies related to CPPS in terms of the number of published literatures, authors, countries, journals, references, and keywords. The results show that UCPPS has attracted the attention of international scholars and there is close collaboration among scholars from various countries. The role of inflammation and oxidative stress in the disease has been the focus of current study and developmental trends in the future research. There is not yet a perfect treatment, further differentiation is needed in clinical work according to the different symptoms, which requires physicians to be flexible enough in their treatment choices to turn to other options when a particular treatment does not work. Paying attention to patient feedback is helpful, and establishing a good feedback platform is part of the effort.

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## Disclosure

Jie Wang and Bin Cao share first authorship. The authors declared that they have no conflict of interest.

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