Diagnosis and treatment of chronic bacterial prostatitis and chronic prostatitis/chronic pelvic pain syndrome: a consensus guideline

Jon Rees,[1] Mark Abrahams,[2] Victor Abu,[3] Trevor Allan,[4] Andrew Doble,[5] Theresa Neale,[6] Penny Nixon,[7] Maxwell Saxty,[8] Sarah Mee,[9] Alison Cooper,[10] Kirsty Haves,[11] and Jenny Lee[12]

[1]GP (Chair of Prostatitis Expert Reference Group), Backwell and Nailsea Medical Group, Bristol; [2]Pain Consultant, Addenbrooke's Hospital, Cambridge; [3]Clinical Nurse Specialist – Prostate, University College London Hospitals, London; [4]Patient Representative; [5]Consultant Urologist, Addenbrooke's Hospital, Cambridge; [6]Urology Clinical Nurse Specialist, South Warwickshire Foundation Trust; [7]Physiotherapist Specialist, Addenbrooke's Hospital, Cambridge; [8]Cognitive Behavioural Therapist, Addenbrooke's Hospital, Cambridge; [9]Policy and Evidence Manager, Prostate Cancer UK; [10]Senior Research Analyst, Prostate Cancer UK; [11]Senior Account Manager, Hayward Medical Communications; [12]Project Manager, Hayward Medical Communications

A **quick reference guide** version of this guideline can be downloaded from:
www.prostatecanceruk.org/prostatitisguideline

ENDORSED BY

BAUN BRITISH ASSOCIATION of UROLOGICAL NURSES

BASHH

September 2014

(due for review September 2017)

PROSTATE CANCER UK

Helping more men survive prostate cancer and enjoy a better quality of life

Contents

Introduction

Overview

Chronic bacterial prostatitis (CBP) and chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) are common, debilitating conditions, with 35–50% of men reported to be affected by symptoms suggestive of prostatitis at some time in their life.[1,2] However, as a result of significant overlap of symptoms with other conditions, such as benign prostatic hyperplasia (BPH) or prostate cancer, estimates of true prevalence are limited.[2,3] Based on a population of over 10,600 participants, a systematic review found a population-based prevalence of prostatitis symptoms of 8.2% (range 2.2–9.7%).[1] CP/CPPS is the most common category of prostatitis.[4,5] The condition affects men of all ages, although it is most prevalent among those aged 36–50 years, shows no apparent racial predisposition and is significant both in terms of symptom burden and cost.[6]

CBP and CP/CPPS show heterogeneity in terms of clinical manifestations, which arise from a variety of possible underlying aetiologies.[7,8] These aetiological mechanisms include:[3]

- Infection
- Anatomical
- Genetic
- Endocrine
- Neuromuscular
- Immunological
- Psychological.

The main four symptom domains of CBP and CP/CPPS are urogenital pain, lower urinary tract symptoms (LUTS), psychological issues and sexual dysfunction.[9] The most common presentation of CBP is recurrent urinary tract infection (UTI), whereas pain is a predominant symptom of both CBP and CP/CPPS.[9,10] This can be nociceptive (for example, caused by physical dysfunction and/or inflammation); however, a growing body of evidence suggests that pain symptoms in CP/CPPS may be neuropathic in nature[3,11,12] and are caused by dysfunction of the somatosensory nervous system.[13] While a proportion of the pain symptoms experienced by patients with CP/CPPS may derive directly from the prostate, it should be noted that pain symptoms are frequently generated by other structures within (and outwith) the pelvis, including muscles, nerves and bony structures within the pelvis, abdomen and spine.

CBP and CP/CPPS have a significant impact on patients' quality of life (QoL)[14] and present diagnostic and therapeutic challenges for physicians. However, relatively little attention has been drawn from urologists or the wider medical community when compared with other urological conditions and they are, therefore, underrepresented in the

literature.[2] The absence of robust and clear epidemiological data in the literature may also result from the lack of a uniform definition and the overlap of symptoms with other conditions such as BPH and prostate cancer. The classification system used most commonly is that of the National Institutes of Health (NIH) (see **Table 1**), which highlights an important point: that although the description 'prostatitis' suggests the presence of infection and inflammation, this is not always the case.

Table 1. NIH classification and definition of the categories of 'prostatitis'[15]

NIH classification	Definition
I: Acute bacterial prostatitis	• Acute infection of the prostate gland
II: Chronic bacterial prostatitis	• Chronic or recurrent infection of the prostate
III: Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS)	• No demonstrated infection
IIIa: Inflammatory CPPS[a]	• White cells in semen and/or EPS or VB3 after prostatic massage
IIIb: Non-inflammatory CPPS[a]	• No white cells in semen/EPS/VB3
IV: Asymptomatic inflammatory prostatitis	• No subjective symptoms detected • Inflammation shown either by prostate biopsy or the presence of white cells in EPS/semen during evaluation for infertility or other disorders

CP = chronic prostatitis; CPPS = chronic pelvic pain syndrome; EPS = expressed prostatic secretions; NIH = National Institutes of Health; VB = voided bladder; VB3 = post-prostatic massage voided bladder urine

[a] During CP/CPPS, it is possible for patients to switch between the two subcategories (IIIa and IIIb), but this has little effect on their subsequent clinical management.

Guideline objectives

A Prostatitis Expert Reference Group (PERG) was convened by Prostate Cancer UK to develop a consensus guideline to improve the diagnosis and management of adult men with CBP (NIH category II) and CP/CPPS (NIH category III).

The main objectives of the guideline are to:

- provide guidance to healthcare professionals treating patients with CBP and CP/CPPS, both in non-specialist (for example, primary care) and specialist (for example, secondary care) settings
- improve non-specialists' awareness and recognition of CBP and CP/CPPS
- promote the efficient referral of care between non-specialists and specialists and the involvement of the multidisciplinary team (MDT)
- facilitate the improvement of patient awareness and recognition of CBP and CP/CPPS.

A quick reference guide of the guideline, which contains the priorities of implementation and main treatment recommendations, can be downloaded from www.prostatecanceruk.org/prostatitsguideline.

The information held within this guideline will complement the evidence base described within other major publications in this therapy area, which are signposted in **Appendix A**.

Guideline population

This guideline only covers symptomatic, chronic forms of the condition; thus, the patient populations under the NIH classification categories I (acute bacterial prostatitis) and IV (asymptomatic inflammatory prostatitis) were not considered during guideline development. By definition, a diagnosis of CBP (NIH category II) or CP/CPPS (NIH category III) should be based on a history of persistent or recurrent symptoms, and the absence of other urogenital pathology (for example, active urethritis, urogenital cancer, urinary tract disease), for a minimum of three out of the past six months.[3,16-18]

Methods

Prostatitis Expert Reference Group

Under the direction of Prostate Cancer UK, members of the PERG were invited from a network of clinical experts in the urology field across a broad range of disciplines, including primary care, urology (medical and nurse specialists), pain, physiotherapy and psychology, from across England. In addition, the PERG included a technical team of representatives from Prostate Cancer UK and Hayward Medical Communications, who had a background in communication, policy development and evidence research. The full details of PERG members are provided in **Appendix B**. The PERG met four times during the guideline development process:

- At Meeting 1, the group discussed its objectives and reviewed the proposed search terms for the literature/evidence search to determine the scope of the guideline and agree search terms
- At Meeting 2, the group discussed the literature review outcomes and agreed the next steps in the development of the guideline
- At Meeting 3, the group reviewed and discussed the draft guideline materials that had been developed
- At Meeting 4, the group reviewed the final materials and agreed on the next steps for implementation and endorsement of the guideline.

The meetings were face-to-face, wherever possible, with participants who were unable to attend in person participating via teleconference or videoconference. In addition, between meetings, project progress was discussed regularly and members of the PERG were involved via email in providing input to the guideline development.

Literature search

Search protocol

A literature search was completed to identify published literature on the diagnosis and management of CBP and CP/CPPS from 1999[*] to the present day (searches completed on 7 February 2014). For the intervention search concepts, the search was designed to retrieve randomised controlled trials (RCTs), observational studies, case-control studies, guidelines, systematic reviews and meta-analyses. For the diagnosis and signs and symptoms search concepts, review articles (excluding comment articles) were also consulted. The primary database searched was Medline (via PubMed); additional sources included the Cochrane Library and professional guideline groups, including the National Institute for Health and Care Excellence (NICE) and the European Association of Urology (EAU). The full literature search protocol is described in **Supplementary Appendix 1**.

[*] The year of 1999 was chosen for the literature search as this was when clinical trials started reporting patients' symptoms using the validated National Institutes of Health Chronic Prostatitis Symptom Index tool

Level of evidence

References used in the guideline text have been assessed according to the Oxford Centre for Evidence-based Medicine (OCEBM) Levels of Evidence (see **Table 2**).[19] The purpose of grading evidence is to provide transparency on the weight of evidence used to inform the recommendations. All major guideline recommendations made in this document are in bulleted and bold text, with the level of evidence denoted in brackets.

Table 2. Level of evidence[a]

Level	Type of evidence
1	Evidence obtained from meta-analysis of randomised trials
2	Evidence obtained from at least one well-designed randomised controlled study
3	Evidence obtained from non-randomised control cohort or follow-up study
4	Evidence obtained from case series, case-control studies, or historically controlled studies
5	Evidence obtained from mechanism-based reasoning, expert committee reports or opinions or clinical experience of respected Authorities

[a] Modified from OCEBM Levels of Evidence Working Group[19]

Delphi panel

Process

Due to the limited number of published RCTs in CBP and CP/CPPS, the PERG concluded that the guideline would benefit from a supporting web-based Delphi panel. This is an anonymous group technique, which is an iterative process, designed to gather individual opinions from experts and transform these into a group consensus.[20] A Delphi panel was conducted to form consensus recommendations in relation to the CBP and CP/CPPS, in areas where high quality, published evidence is currently lacking.

Delphi participants were invited into the process if they had a strong interest or specialism in managing patients with CBP and/or CP/CPPS and were recruited via the clinical networks of PERG members. A number of different specialists relevant to the MDT were invited to participate, including GPs, urologists, pain specialists, nurse specialists, physiotherapists, cognitive behavioural specialists and sexual health specialists. The web-based Delphi process comprised three questionnaire rounds, which were delivered via the Survey Monkey® platform. Consensus in the responses was defined as an agreement of at least 70% from the respondents (after excluding 'not relevant to my expertise' responses). After each round, any questions that achieved consensus were removed from the next survey round. In cases where consensus was not gained, statement refinement was completed using information from the free-text comments provided by Delphi participants and input from the PERG and a supporting technical team. The free-text comments from Delphi participants were also used to generate additional questions for inclusion in

subsequent survey rounds. After each round, Delphi participants were provided with a summary of anonymised results, to allow each participant to reflect on their own individual answers in the context of all responses.

Results

Excluding the participant screening questions (eg, on specialism and geographical location), a total of 46, 20 and seven questions were included in the first, second and third survey rounds, respectively. Questions included a mixture of treatment statements that required rating ('agree', 'neutral' or 'disagree'), multiple-choice questions (both tick-one and tick-all that apply) and requests for free-text input. A full description of all questions can be downloaded from www.prostatecanceruk.org/prostatitisguideline. The survey was circulated to 58 participants, of which 35 (60%), 29 (50%) and 26 (45%) responded to the first, second and third rounds, respectively. Only participants who responded to the first round where invited into the second round, and only those who responded to the second round were invited into the third round. Delphi panellists came from multiple regions across the UK and a small number (two) were based in North America. All treatment statements that achieved consensus are incorporated within the recommendations below. Statements that did not reach consensus are also mentioned in the appropriate treatment subsections, for transparency.

Priorities for implementation

In addition to the main treatment recommendations made in this guideline, which are described in the subsequent sections, the PERG concluded the following areas as priorities for implementation:

1. **Patients with CBP or CP/CPPS should be managed according to their individual symptom pattern – no single management pathway is suitable for all patients with these conditions.**

2. **Most patients with CP/CPPS do not have an infection, and repeated use of antibiotics such as quinolones should be avoided where no obvious benefit from infection control is evident or cultures do not support an infective aetiology.**

3. **Early use of antineuropathic pain medication should be considered for all CBP and CP/CPPS patients refractory to initial treatments. If neuropathic pain is suspected, ensure a quick referral to the MDT, which includes pain specialists.**

4. **Early referral to specialist services should be considered when patients fail to respond to initial measures. Referral should ideally be to a clinician with an interest in the management of CBP and/or CP/CPPS, but not necessarily a urologist.**

5. **An MDT approach should be implemented and made available to CBP and CP/CPPS patients. The MDT should include urologists, pain specialists, nurse specialists, specialist physiotherapists, GPs, cognitive behavioural therapists/psychologists and sexual health specialists.**

6. **Patients should be fully informed about the possible underlying causes and treatment options of CBP and CP/CPPS. The MDT responsible for the management of these patient groups, should be able to explain the chronic pain cycle and other relevant information to improve patient understanding of the conditions.**

Management recommendations – initial presentation

Introduction

Figure 1 provides a treatment algorithm to guide the management of patients with suspected or confirmed CBP or CP/CPPS. This algorithm is based on a combination of evidence from the literature, consensus obtained via the Delphi panel process and consensus obtained from members of the PERG. The evidence and reasoning behind this algorithm are discussed below.

To aid with the position of recommendations within the presented algorithm, consensus was sought on what duration of symptoms and antibiotic status of a patient constituted 'early-stage' versus 'late-stage' CBP or CP/CPPS. This definition can help inform when patients would typically be offered earlier lines versus later lines of treatment options. Decisions regarding choice of treatment should, however, ultimately be based on a symptom-led approach.

- **CBP or CP/CPPS patients could be considered to be in the 'early stages' of the disease if they have experienced persistent, recurrent symptoms for less than six months and are antibiotic-naive (Level 5).**
- **CBP or CP/CPPS patients could be considered to be in the 'later stages' of the disease if they have experienced persistent, recurrent symptoms for over six months and are refractory to initial lines of pharmacotherapy (Level 5).**

Signs and symptoms

CBP and CP/CPPS show heterogeneity of clinical manifestations arising from the variety of possible underlying aetiologies (for example, bacterial infection and/or inflammation and/or neurological damage) and symptoms can vary between patients or fluctuate over time.[7,8] The four main symptom domains associated with CBP and CP/CPPS are urogenital pain, LUTS, psychological issues and sexual dysfunction,[9] which are fully or partially assessed by the NIH Chronic Prostatitis Symptom Index (NIH-CPSI).[21] Tests for correlations between the NIH-CPSI symptom domains suggest that urogenital pain has a greater impact on patients' QoL than urinary symptoms.[10]

Patients with urogenital pain symptoms can experience pain or discomfort in the perineal, suprapubic, scrotal, testicular, penile, lower back, abdominal, inguinal or rectal regions.[17,22] In addition, they may report dysuria, or pain during or after ejaculation.[17] Findings from a retrospective analysis of clinical records (n=1,563) indicate that the most prevalent localisation for pain is the perineal region (63% of patients), followed by the testicular, pubic and penile areas.[10] Tenderness in the abdominal/pelvic region is also reported by patients with CP/CPPS, with the most common sites including the prostate and pelvic floor muscles.[23,24] Irritable bowel syndrome (IBS) has been shown to be present in 22–31% of patients with CBP or CP/CPPS,[25,26] and a co-morbidity of IBS can increase the severity of pain

symptoms experienced by CBP and CP/CPPS patients.[25-27] Neuropathic pain is also a feature of CP/CPPS and is described in more detail in **Box 1**.

LUTS are also a common clinical presentation,[4,22,28] with cohort studies reporting at least one such symptom in 39–68% of patients.[4,29] LUTS include voiding symptoms (for example, weak stream, straining and hesitancy) or storage symptoms (for example, urgency with or without urgency incontinence, increased urinary frequency, nocturia and dysuria).[17,30] There may also be an association with recurrent UTIs in a minority of patients.[5,31]

CBP and CP/CPPS can also have a significant negative impact on patients' QoL; for example, symptoms may cause limitations to activity[18] and the QoL of patients with CBP or CP/CPPS has been shown to be as poor as that of patients suffering from congestive heart failure or Crohn's disease.[14] Negative behavioural consequences and psychosocial symptoms, such as depression and anxiety, can also have a significant impact.[3,16] Small (n<250) case-control studies indicate that depression, anxiety and panic disorder are significantly more common in men with chronic symptoms compared with controls, using responses to the Patient Health Questionnaire (PHQ)[32] or other psychometric questionnaires (for example, the Perceived Stress Scale).[33-35] Furthermore, a small (n=61) cohort study suggests CP/CPPS patients can experience pain catastrophising – a negative cognitive-affective response to anticipated or actual pain – and those with a high tendency towards catastrophising may experience more severe pain and QoL issues and are at risk of developing chronic pain conditions.[36]

Although only partially evaluated by the NIH-CPSI, sexual dysfunction, including symptoms of ejaculatory dysfunction (such as premature, delayed or painful ejaculation), erectile dysfunction (ED) and decreased libido, can also be features of CP/CPPS.[29,35,37-44] Findings from small-to-medium (n=130 to 1,800) cohort studies indicate that total or partial ED is reported by 15–55% of CP/CPPS patients,[38,45-48] while the prevalence of overall, self-reported sexual dysfunction is higher at 46–92%.[38,42,45,48] Correlation studies of sexual dysfunction symptoms with NIH-CPSI scores indicate that CP/CPPS patients with sexual dysfunction have higher total and QoL scores (higher scores indicate more severe symptoms), suggesting sexual symptoms can contribute substantially to the morbidity experienced by men with CP/CPPS.[43,45-47,49,50] However, in one study the presence of ED was shown not to independently affect symptom severity or QoL in CP/CPPS patients.[51]

To summarise the evidence from the literature and consensus discussions held by PERG, patients with CBP and CP/CPPS may present with a variety of symptoms, which may be grouped as follows:

- **Pain symptoms**[10,17,22-24,26]
    - Pain or discomfort in one or multiple urogenital regions including the:
        - Perineum
        - Suprapubic region
        - Testicles

        - Penis (especially penile tip pain)
        - Lower back
        - Abdomen
        - Inguinal region / groin
        - Rectum
    - Pain on urination, or that increases with urination
    - Pain during or after ejaculation
    - Muscle tenderness or dysfunction in abdominal/pelvic regions
    - Neuropathic pain
    - Functional bowel symptoms (eg, IBS)
- **Urinary symptoms**[4,5,17,22,29,52]
    - Voiding LUTS (weak stream, straining and hesitancy)
    - Storage LUTS (urgency with or without urge incontinence, increased urinary frequency, nocturia and dysuria)
    - Urethral burning during, and independent of, micturition
    - Haematospermia (blood in semen)
    - Recurrent UTI (more applicable to CBP)
- **Sexual dysfunction symptoms**[29,35,37-44]
    - ED
    - Ejaculatory dysfunction (premature, delayed or pain during, or after, ejaculation)
    - Decreased libido
- **Psychosocial symptoms**[3,18,32,33,35,36]
    - Anxiety or stress
    - Depression
    - Cognitive/behavioural consequences
    - QoL impact.

Box 1. A description of neuropathic pain in the context of CBP and CP/CPPS

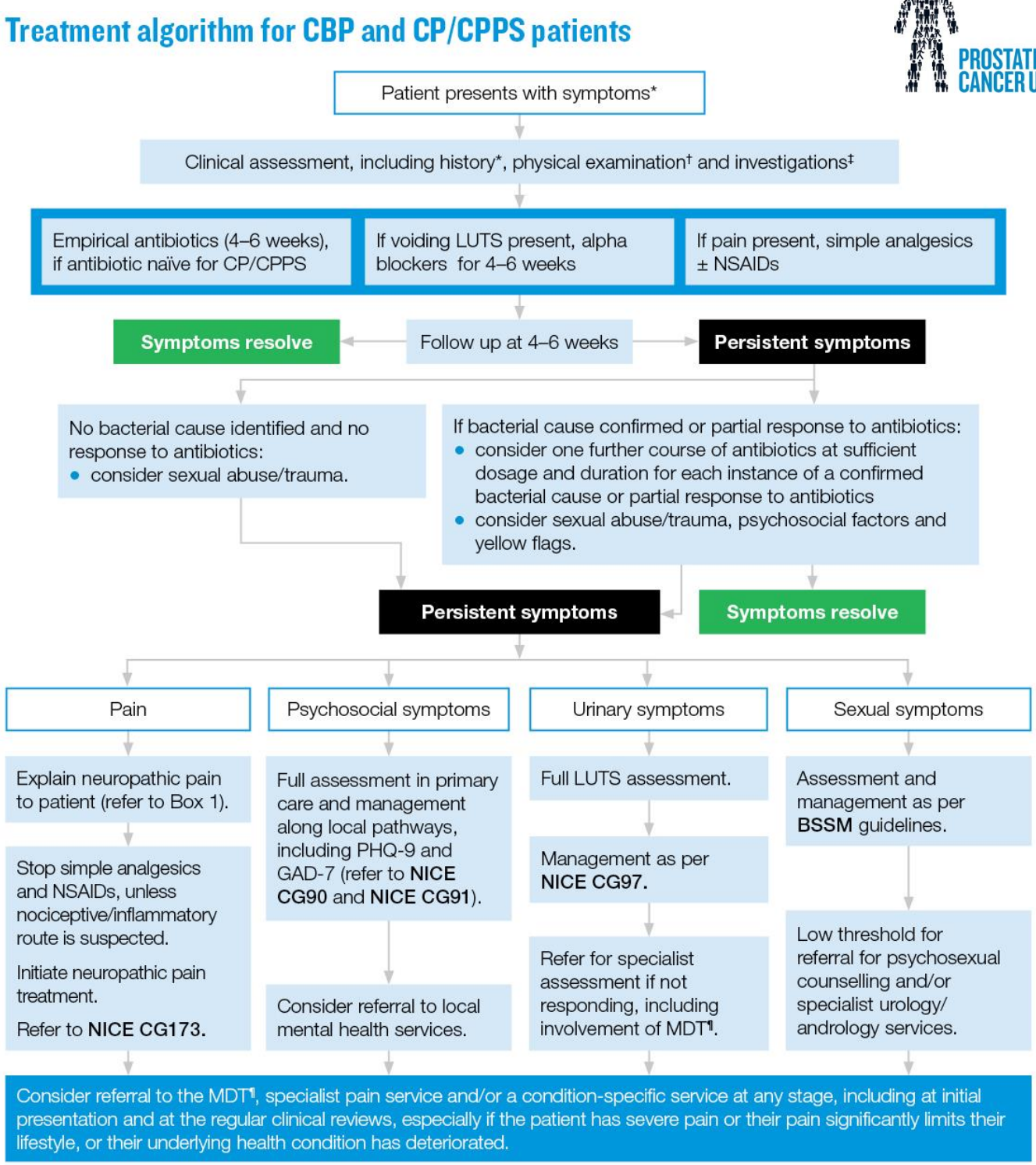
Pain is experienced by the majority, if not all, people across a lifetime and, on most occasions, the pain experienced is in the context of an acute injury or inflammatory process. The body's natural response to pain is to try to protect the injured area, usually by altering posture or muscle tone around this area while the injury, inflammation or infection is healing. Once healing has completed, the pain resolves and any postural and muscular changes return to normal.

However, in a small proportion of people who suffer an injury, inflammation or infection, the sensation of pain continues, despite the resolution or healing of the underlying problem. This sometimes happens because the pain nerves themselves have been damaged by the original injury or inflammation and, as a result, have become sensitised. Other factors that increase the risk of this happening include genetic factors, psychological problems associated with the original injury (eg, anxiety) and prior experience of pain in the injured or inflamed area. In these circumstances, the ongoing pain sensation is due to over-sensitisation of the pain nervous system that supplies the painful area. The pain experienced by the patient is very real, but no longer provides a useful purpose as the injury has already healed or the infection has already resolved.

Thus, in patients with CBP or CP/CPPS, the original infective or inflammatory episode of 'prostatitis' has resulted in sensitisation of the pain nervous system that supplies the prostate and surrounding area. The sensation of pain (which may mimic the original 'prostatitis' pain) continues, despite the fact that, in the vast majority of patients, any underlying infection has completely resolved.

However, the human body will react to pain by trying to protect the painful area, irrespective of whether the signal is due to a genuine injury or an abnormality in the nervous system. If the pain experience is prolonged, these protection mechanisms become entrenched. In the longer term, the changes in posture and muscular function can lead to secondary pain problems, resulting in increased disability and worsening of the pain condition.

Figure 1. Treatment algorithm for CBP and CP/CPPS patients



BSSM = British Society for Sexual Medicine; CP/CPPS = chronic prostatitis/chronic pelvic pain syndrome; GAD-7 = Generalised Anxiety Disorder 7; LUTS = lower urinary tract symptoms; MDT = multidisciplinary team; NICE = National Institute for Health and Care Excellence; NSAIDs = non-steroidal anti-inflammatory drugs; PHQ-9 = Patient Health Questionnaire-9.

* LUTS, including overactive bladder, urgency, hesitancy, slow flow, frequency and storage problems; urethral burning during, and independent of, micturition; pain during micturition; suprapubic pain or discomfort; erectile dysfunction/sexual dysfunction; pain during ejaculation; pain or discomfort in inguinal, rectal, penile, perineal, lumbar regions or abdominal regions; haematospermia (blood in sperm); irritable bowel syndrome; pelvic floor dysfunction and psychosocial yellow flags relating to anxiety, stress and depression.

† Physical examination: abdominal examination, digital rectal examination, external genitalia examination, musculoskeletal assessment.

‡ Investigations (see **Table 3**): urine analysis, four-glass test, sexually transmitted infection screen, tests to rule out differential diagnosis.

¶ Members of the MDT may include: urologist, pain consultant/specialist, nurse specialist, nurse practitioner, physiotherapist, GP, cognitive behavioural/psychological therapist and sexual health specialist.

NICE CG173: www.nice.org.uk/guidance/cg173/resources/guidance-neuropathic-pain-pharmacological-management-pdf
NICE CG90: www.nice.org.uk/guidance/cg90/resources/guidance-depression-in-adults-pdf
NICE CG91: www.nice.org.uk/guidance/cg91/resources/guidance-depression-in-adults-with-a-chronic-physical-health-problem-pdf
NICE CG97: www.nice.org.uk/guidance/cg97/resources/guidance-lower-urinary-tract-symptoms-pdf
BSSM guidelines: www.bssm.org.uk/downloads/BSSM_ED_Management_Guidelines_2013.pdf

Clinical assessment and diagnosis

Patient history

To aid with the clinical assessment of CBP and CP/CPPS, both in terms of initial evaluation and during therapeutic monitoring, a validated symptom-scoring instrument may be used:

- NIH-CPSI – a nine-item questionnaire with a total score of 0 to 43, measuring:
  - Pain (four questions evaluating pain location, frequency and severity, 0 to 21)
  - Voiding (two questions evaluating voiding and storage symptoms, 0 to 10)
  - Impact on QoL (three questions, 0 to 12)
- International Prostate Symptom Score (IPSS) – an eight-item questionnaire measuring:
  - Urinary symptoms (seven questions evaluating incomplete bladder emptying, frequency, intermittency, urgency, weak stream, straining and nocturia, 0 to 35)
  - Impact on QoL (one question, 0 to 6)
- International Index of Erectile Function (IIEF-5) or Sexual Health Inventory for Men (SHIM) – a five-item questionnaire for the screening and diagnosis of ED that takes into account a patient's past six months of symptoms
- Patient Health Questionnaire-2 (PHQ-2) – a two-item questionnaire to assess the frequency of depressed mood over the past two weeks
- Patient Health Questionnaire-9 (PHQ-9) – a nine-item questionnaire to assess the frequency of depressed mood over the past two weeks
- Generalised Anxiety Disorder-7 (GAD-7) – a seven-item questionnaire to assess the severity of generalised anxiety disorder over the past two weeks.

A more recently devised scale, the **U**rinary, **P**sychosocial, **O**rgan-specific, **I**nfection, **N**eurological/systemic, and **T**enderness (UPOINT) scale, aims to stratify patients into specific symptom-led phenotypes.[53] The clinical domains assessed are urinary symptoms, psychosocial dysfunction, organ-specific findings, infection, neurological/systemic routes, and tenderness of muscles.[53] Several patient cohort studies have shown a strong correlation between the number of UPOINT-positive domains and the NIH-CPSI total score.[8,42,54] Furthermore, the UPOINT scale has been used to inform phenotypically directed multimodal treatment in CP/CPPS patients, with 84% of patients reporting at least a six-point fall in NIH-CPSI scores.[55] However, a lack of correlation between the number of positive UPOINT domains and the IIEF-5[54] has led to the suggestion that the addition of a sexual dysfunction[42] or ED[8] domain to UPOINT would assist with the evaluation of patients.

Based on the current published literature, the consensus recommendation of the PERG was as follows:

- **Reliable instruments, such as the NIH-CPSI, IPSS and UPOINT scales, should be considered to assess initial symptom severity, evaluate phenotypic differences and monitor patients' response to therapeutic intervention (Level 3).**

Due to the significant impact that CBP and CP/CPPS can have on an individual's QoL[14] and the possibility of negative behavioural consequences,[3,4,16,33,35] assessment of psychosocial symptoms should be considered. The use of validated questionnaires, such as the PHQ-9, *PHQ-2*, *GAD-7 and the Hospital Anxiety and Depression Scale (HADS), and/or questions to pinpoint psychosocial flags during clinical assessment, should be considered (see* ***Box 2****). Findings from an epidemiological survey have shown that m*en who reported a previous history of sexual, physical or emotional abuse were more likely to have symptoms suggestive of CP/CPPS. In addition, previous abuse increased both the NIH-CPSI pain and urinary scores.[56] In light of these findings, screening for major trauma events should also be considered (see **Box 2**). The Delphi approach was used to reach a consensus on the implementation of psychosocial screening for CBP and CP/CPPS patients:

- **CBP and CP/CPPS patients should be screened for psychosocial symptoms (eg, anxiety or stress) using either the psychosocial yellow flag system and/or PHQ-9 and/or GAD-7 scales. If a clinically relevant level of psychosocial symptoms is observed, referral to a psychosocial specialis[†] should be considered as a treatment option (Level 5).**

Box 2. Assessment of psychosocial flags

Validated questionnaires
- Patient Health Questionnaire-9 (PHQ-9)
- Patient Health Questionnaire-2 (PHQ-2)
- Generalised Anxiety Disorder-7 (GAD-7)
- Hospital Anxiety and Depression Scale (HADS)

Initial presentation questions
Anxiety screening questions: In the last month, have you often been bothered by:
- Feeling nervous, anxious or on edge?
- Not being able to stop or control worrying?

Depression screening questions: In the last month, have you often been bothered by:
- Feeling down, depressed or hopeless?
- Having little interest or pleasure in doing things?

Treatment-refractory patient questions
Life event screening questions:
- Have you recently undergone any major life events; eg, moving house, divorce, bereavement or change of job/career?

Trauma and abuse screening questions:
- When growing up, or more recently, have any relationships been difficult or have situations happened that you have found yourself uncomfortable with?

[†] eg, psychiatrist, specialist psychologist or cognitive behavioural therapist

Patient communications

During clinical assessment of CBP and CP/CPPS, it is important that the diagnosis, aetiology and management approaches are discussed with the patient; consensus gained via the Delphi approach recommends the following:

- **At first presentation, other concerns or differential diagnoses, including urological cancers and infertility, should be discussed with the patient to establish a full patient history and help inform future investigations (Level 5).**
- **When diagnostic tests for a bacterial cause of CBP or CP/CPPS have been confirmed, the results need to be clearly communicated to the patient; the patient must be clearly informed of both positive and negative results of diagnostic tests and what the results mean for their future treatment options (Level 5).**
- **CBP and CP/CPPS patients who present in either a non-specialist or a specialist setting should be informed of the underlying cause of CBP and CP/CPPS to help improve patient understanding of the condition. This may include an explanation of the chronic pain cycle, the routes of pain (neuropathic versus nociceptive) and the basic anatomy of the pelvic region (eg, position of the pelvic floor muscle) (Level 5).**

Reliable sources for patient information include those available through the Prostate Cancer UK website:

- *'Prostatitis: A guide to infection or inflammation of the prostate'* – provides patient information on prostatitis, including a description of the causes, symptoms, diagnosis and treatment of prostatitis
- *'Understanding the PSA test: A guide for men concerned about prostate cancer'* – provides patient information with respect to the prostate-specific antigen (PSA) test for men concerned about prostate cancer
- *'Know your prostate: A guide to common prostate problems'* – provides patient information with respect the prostate gland and what symptoms to look out for. This booklet includes information on prostate cancer, enlarged prostate (BPH) and prostatitis.

Physical examinations

Examinations to assess the physical changes and signs of CBP and CP/CPPS, as well as to exclude other possible urogenital pathologies, include the following:[3,17,18]

- Abdomen and external genitalia assessment
  - Bladder may be palpable if there is urinary retention
- Digital rectal examination (DRE)
  - The prostate may be enlarged, tender, or normal
- Pelvic floor examinations
  - The perineum and superficial pelvic floor muscles may be palpated externally and the deep muscles internally via the rectum

- The quality, timing, strength and endurance of the pelvic floor muscles are tested in addition to the ability to fully relax the muscles between contractions
- Muscular pain, tightness and trigger points may be palpated on examination

- Musculoskeletal examination
  - Check that symptoms are not being provoked by other structures.

Investigations

A summary of the investigations and physical examinations that should be considered during clinical assessment, including whether they are considered as a core or optional part of the clinical assessment and in which setting (eg, non-specialist versus specialist) they are typically completed in, is detailed in **Table 3**.

Options for laboratory diagnosis include the collection of a midstream specimen of urine (MSU) for analysis via urine dipstick and/or culture to confirm the presence of UTI and/or haematuria.[16,17] However, to evaluate if there is a bacterial cause to the condition, the four-glass (Meares–Stamey) test is considered the gold standard for diagnosis (or exclusion) of CBP, whereby voided bladder (VB) urine (VB1, VB2 and VB3) and expressed prostatic secretion (EPS) samples are taken for culture/microscopy (see **Table 3**).[18,57] The two-glass test (VB2 and VB3) has been shown to offer similar diagnostic sensitivity in a comparison study with the four-glass test,[52] while other studies advocate the use of urethral swab plus a post-prostatic massage urine analysis (VB3).[58] Additional information with respect to a bacterial cause may also be obtained from the culture and microscopy of a semen sample;[18] however, the usefulness of semen culture in CBP diagnosis has been debated, with sensitivity reported at approximately 50%. Semen culture is, therefore, not routinely part of the diagnostic assessment of CBP patients in either specialist or non-specialist settings.[31,57] Furthermore, semen culture in isolation does not take into account possible urethral contamination and is, therefore, misleading. The completion of a sexually transmitted infection (STI) screen, including a nucleic acid amplification test (NAAT) on first-catch urine specimens (for the diagnosis of gonorrhoea and chlamydia), should also be considered to rule out STI.[16]

During clinical investigations, strong consideration should be given to the differential diagnosis, as the symptoms of CBP and CP/CPPS significantly overlap with those of other conditions.[16-18] PSA testing should be considered (after adequate counselling regarding the test) to rule out prostate cancer under the following circumstances: abnormal prostate on DRE, patient concern in relation to prostate cancer, or when symptoms are suggestive of bladder outlet obstruction (BOO) secondary to benign prostatic enlargement (BPE).[16-18] It is important to bear in mind that PSA levels may be falsely elevated during an active phase of prostatitis – testing should, therefore, be avoided at such a time, if possible, or the results interpreted with caution. The particular characteristics of PSA testing (that is, timing restriction of the test in relation to current/previous treatment and age-specific results for prostate cancer risk management) are shown in **Box 3**. Conditions to be excluded are:

- Urogenital/urological cancer (eg, prostate or bladder)

- Rectal cancer
- Prostatic abscess
- Urinary tract disease (eg, cystitis, urethritis or upper UTI)
- Urethral stricture
- BPE
- Obstructive calculus or foreign body
- Pudendal neuralgia
- Unilateral or bilateral epididymo-orchitis
- Prostate tuberculosis
- Neurological disease affecting the bladder.

Investigations that should be considered to rule out the above are detailed in **Table 3**.

Table 3. Summary of physical examinations and investigations to consider during the clinical assessment of CBP and CP/CPPS

Examinations and investigations[a]	Setting		Rating	
	Non-specialist	Specialist	Core	Optional
Physical examinations				
Digital rectal examination • Including assessment of external genitalia and pelvic floor muscle dysfunction	✓	✓	✓	
Abdomen • To exclude other causes of abdominal pain	✓	✓	✓	
Urine dipstick and/or MSU for culture/microscopy	✓	✓	✓	
Four-glass or two-glass test:[b] VB1 – voided bladder 1 • Represents the urethra VB2 – voided bladder 2 • Represents the bladder EPS – expressed prostatic secretions • Represents the prostate VB3 – voided bladder 3 • Represents the prostate		✓		✓
Tests to rule out differential diagnoses:[c]				
PSA testing to exclude prostate cancer (refer to **Box 3**)	✓	✓	✓	
STI screen (eg, via NAATs)	✓	✓	✓	
Uroflowmetry, retrograde urethrography or cystoscopy (to exclude BOO, urethral stricture or bladder neck stenosis)		✓		✓
Prostate biopsy (only if prostate cancer is suspected on basis of PSA and/or DRE results)		✓		✓
Transrectal ultrasound (only in refractory patients in whom a prostatic abscess or other pathology is suspected)		✓		✓
Diagnostic cystoscopy if bladder cancer is suspected		✓		✓
Urethral swab and culture if urethritis is suspected		✓		✓
MRI if prostatic abscess suspected		✓		✓

[a] Based on information adapted from Map of Medicine. Prostatitis – Primary Care, January 2014,[17] Map of Medicine. Prostatitis – Secondary Care, January 2014,[18] Nickel *et al,* 2003[59] and PERG consensus.
[b] Pursued when CBP is suspected.
[c] The investigations pursued will depend on symptom presentation and patient history.
NB Local provider services may vary with respect to the division of assessment options across non-specialist and specialists settings. Abbreviations: BOO = bladder outlet obstruction; CBP = chronic bacterial prostatitis; CP/CPPS = chronic prostatitis/chronic pelvic pain syndrome; MRI = magnetic resonance imaging; MSU = midstream urine; NAATs = nucleic acid amplification tests; PSA = prostate-specific antigen; STI = sexually transmitted infection.

Box 3. PSA test[a]

Timing:
PSA testing should be postponed for:
- Six weeks after treatment for a UTI
- One week after a DRE
- 48 hours after vigorous exercise or sexual activity
- Six weeks after a prostate biopsy
- Two weeks after flu-like symptoms

Age-specific cut-off PSA measurements for prostate cancer risk management:
- Age 50–59 years – greater than or equal to 3.0 ng/ml
- Aged 60–69 years – greater than or equal to 4.0 ng/ml
- Aged 70 years and older – greater than or equal to 5.0 ng/ml
- There are no age-specific ranges for men aged 80 years and older
- Refer to local laboratory upper limits of normal

Treatment effects
- If assessing PSA levels in a patient on a 5-alpha-reductase inhibitor, note that a decrease in PSA levels is seen rapidly within the first few months of treatment. After six months of 5-alpha-reductase inhibitor treatment, PSA levels will have decreased by approximately 50%, setting a new baseline – any subsequent rises from this level should be considered abnormal
- PSA levels may be falsely elevated during an active phase of prostatitis. Avoid testing at these times, if possible, or interpret results with caution

Interpret PSA results with care
Take caution with results interpretation, since PSA levels are prostate- rather than prostate cancer-specific and levels can be elevated with:
- Prostate enlargement
- Prostate cancer
- Infection or inflammation
- Physical causes – vigorous exercise (eg, cycling), DRE, prostate biopsy
- A normal prostate

DRE = digital rectal examination; PSA = prostate-specific antigen; UTI = urinary tract infection

[a] Adapted from information with the Prostate Cancer Risk Management Programme.[60] The Prostate Cancer UK booklet 'Understanding the PSA test' provides relevant patient information with respect to PSA testing

Diagnosis

To establish a diagnosis of CBP or CP/CPPS, the patient should, by definition, have a history of persistent or recurrent symptoms, and the absence of other urogenital pathology (for example, active urethritis, urogenital cancer, urinary tract disease), for a minimum of three out of the past six months.[3,16-18] However, some men have fluctuating symptoms and, in practice, the diagnosis is often suspected after a shorter duration of symptoms.[16]

A definitive diagnosis of CBP relies on the presence of (typically recurrent) UTI and isolation of an aetiologically recognised organism from prostatic fluid or urine.[16,18] However, in many cases, patients respond to antibiotic intervention in the absence of a confirmed infection – in such cases, a CBP diagnosis can be suspected but is not certain, since the response may be due to the anti-inflammatory or antineuropathic effect of the antimicrobial agent. There is no gold standard for a definitive diagnosis of CP/CPPS; instead, it is typically based on a patient history, symptoms and the exclusion of other causes (for example, non-demonstrable infection and other urogenital/urological pathology).[16]

Referral to a specialist setting

To ensure appropriate access to specialist care is provided, referral to specialist care should be considered at initial presentation in the following instances:[17]

1. If there is diagnostic uncertainty in relation to the possible differential diagnosis
2. In the presence of severe symptoms that require immediate specialist attention.

Treatment strategies

Alpha-blockers

From the literature, ten RCTs (n=58 to 272) were identified that evaluated alpha-blockers versus placebo in the treatment of CBP and CP/CPPS, covering tamsulosin,[61-63] alfuzosin[64,65] doxazosin,[66,67] terazosin[68,69] and silodosin.[70] The majority (eight out of ten) of these RCTs showed positive results for alpha-blockers, with significant differences compared with placebo in NIH-CPSI total, urinary symptom, pain, and/or QoL scores[62-65,67,68] or significant differences observed with the use of other validated symptom scoring tools.[66 69] However, the design of the RCTs identified varied in terms of primary endpoints, patient eligibility criteria (for example, pre-exposure to alpha-blockers) and trial duration (six weeks to six months). Despite these methodological differences, these findings, taken together, have contributed to widespread use of alpha-blockers in the treatment of CBP and CP/CPPS in recent years. Indeed, a recent systematic review and network meta-analysis of alpha-blocker RCTs showed significant differences compared with placebo in total, pain, voiding and QoL NIH-CPSI scores.[71] However, another recent systematic review provided contrasting conclusions and the authors questioned whether the observed reductions were on a scale that was clinically significant.[72] High heterogeneity was found between trials in both these meta-analyses, which was attributed to publication bias due to small-study effect[71] or due to the differing trial designs.[72]

Notably, two of the larger, placebo-controlled trials that evaluated tamsulosin (n=196)[61] and alfuzosin (n=272)[65] failed to show any significant difference in total NIH-CPSI scores, the only outcome achieving statistical significance being the score for ejaculation of the Male Sexual Health Questionnaire (p=0.04) in the alfuzosin trial. It has been postulated that possible reasons for these 'negative' results were the short treatment duration (up to 12 weeks) and/or the inclusion of refractory patients with pre-exposure to alpha-blockers.[65]

Based on the current published literature, the consensus treatment recommendation of the PERG was as follows:

- **Alpha-blockers may have a modest treatment effect regarding total, urinary symptom, pain and QoL scores in CBP and CP/CPPS and should be considered as an initial treatment option (Level 1).**

Although evidence from RCTs largely points to alpha-blockers providing an improvement in clinical outcomes, there is a lack of evidence to inform best practice with respect to the duration of treatment or first-line versus second-line options. In addition, there is a lack of published evidence to suggest a phenotypically directed approach (for example, offered to patients with voiding dysfunction as a major symptom). The Delphi approach was, therefore, used to reach a consensus on what is considered to be best practice with respect to offering alpha-blockers to patients with CBP or CP/CPPS. The consensus of the Delphi panel was as follows:

- **Treatment with alpha-blockers should be considered in CBP and CP/CPPS patients who present with significant voiding LUTS (eg, slow urinary flow, hesitancy) (Level 5).**
- **If no relief from voiding LUTS or other symptoms of CBP or CP/CPPS is achieved with alpha-blockers within four to six weeks, treatment should be stopped and a different pharmacotherapy should be considered or patients should be referred to specialist care if other approaches have been exhausted (Level 5).**
- **Due to the side effect profiles of alpha-blockers, consider offering uro-selective[‡] alpha-blockers as first line in CBP and CP/CPPS patients who present with voiding LUTS (Level 5).**

[‡] Uro-selective alpha-blockers include tamsulosin, alfuzosin and silodosin

Antibiotics

A wide spectrum of strains may cause infection in CBP (see **Box 4**). While there is general consensus on the role of bacteria such as *E. coli*, *P. mirabilis*, *K. pneumoniae* or *P. aeruginosa* in CBP, the significance of some bacteria, such as *C. trachomatis*, to the condition remains uncertain.[22,73,74] However, small-to-medium (n=55 to 261) observational studies have suggested a role for *C. trachomatis*[73,75-77] and other 'non-traditional' bacteria[74,78] in the aetiology of CBP. Other organisms such as *M. tuberculosis*, *Candida* species and rare pathogens, including *Coccidioides immitis*, *Blastomyces dermatitidis*, and *Histoplasma capsulatum,* may cause CBP in those with immunodeficiency.[22]

Box 4. Pathogens in prostatitis[a]

Aetiologically recognised pathogens
Escherichia coli
Klebsiella spp.
Proteus mirabilis
Enterococcus faecalis
Pseudomonas aeruginosa

Organisms of debatable significance
Staphylococci
Streptococci
Corynebacterium spp.
Chlamydia trachomatis
Ureaplasma urealyticum
Mycoplasma hominis

[a] Adapted from Grabe *et al,* 2013[22]

Despite the wide use of antibiotics in the treatment of patients with CBP and CP/CPPS, the evidence-base for their use in these populations is relatively weak. The evidence in a CBP population primarily exists within randomised comparative trials or retrospective comparative trials that lack a placebo control. These studies report microbiological eradication rates of 40% to 77% for ciprofloxacin,[76,79,80] 75% for levofloxacin,[79] 80% for azithromycin,[75-77] 77% for doxycycline,[75] 80% for clarithromycin[77] and 62% to 77% for azithromycin plus ciprofloxacin (depending on ciprofloxacin dose).[81] Higher eradication rates (>90%) were reported when using azithromycin and levofloxacin either alone, in combination or sequentially, depending on the locality of infection (urethral, prostatic or both), specifically in CBP patients with a *C. trachomatis* infection.[73] As assessed by changes in NIH-CPSI scores, significant differences in symptom severity were observed between baseline and the end of treatment in two trials.[73,81] Others reported improvement in clinical outcomes but failed to use validated tools to report these.[75-77,79,80]

Of the identified comparative studies in patients with CBP, one (n=408) suggests levofloxacin offers advantages over ciprofloxacin in terms of bacterial eradication rates and clinical improvement,[80] while another of similar size (n=377) and design showed no significant differences between these agents.[79] In terms of interclass observations, Skerk and colleagues showed azithromycin had better efficacy compared with ciprofloxacin, specifically in the treatment of *C.*

trachomatis infections.[76] Although there is a lack of prospective, head-to-head placebo-controlled trials to assess intraclass and interclass antibiotic comparisons, each class is associated with its own advantages and caveats, which are described in **Table 4**. The quinolones, such as ciprofloxacin and levofloxacin, are considered the antibiotics of choice because of their favourable pharmacokinetic properties.[22] Another antibiotic agent, fosfomycin, has reasonable intraprostatic tissue levels and is active against extended-spectrum beta-lactamase producers; it can be considered in patients with multi-resistant Gram-negative infections, based on susceptibility results and discussion with local microbiologists.

Only three small-to-medium sized (n=48 to 196), adequately designed RCTs, which assessed ciprofloxacin,[61] levofloxacin[59] and tetracycline hydrochloride[82] versus placebo in CP/CPPS patients, were identified. Although symptom improvement was observed, the ciprofloxacin study failed to show a statistical difference in NIH-CPSI total score from baseline to six weeks in a CP/CPPS population.[61] Similar results were observed in the levofloxacin study; while symptom improvement with antibiotic treatment was observed, the results failed to achieve significance against placebo, both at end of treatment (six weeks) and at follow-up (12 weeks) versus baseline.[59] However, the patient cohorts within these studies had been diagnosed with CP/CPPS on average for 6.2 years[61] and 6.5 years[59] at study enrolment. Such patients may represent a treatment-refractory phenotype for which antibiotic therapy may not be appropriate. The low patient numbers may also have contributed to the lack of significance. More promising results were observed in a tetracycline hydrochloride versus placebo study, where significant differences in NIH-CPSI scores and bacterial eradication rates were reported; however, patient numbers were small (n=48).[82] Recent direct meta-analyses of these trials showed that antibiotics provide symptom improvement, but not at a significant level.[71,72] Evidence from small (n=20 to 105), randomised, comparative trials provides mixed support for using antibiotics in CP/CPPS, with significant differences from baseline in symptoms observed using levofloxacin[83] but not ciprofloxacin;[84] however, the ciprofloxacin study imposed a stringent significance threshold ($p<0.001$).

Based on the current published literature, the consensus treatment recommendations of the PERG were as follows:

- **Antimicrobial therapy may have a moderate effect on total, urinary, pain and QoL scores in CBP and CP/CPPS and should be considered as an initial treatment option (Level 1).**
- **Antimicrobial therapy should be guided by bacterial cultures and sensitivities, while accounting for any drug interactions and/or contraindications (Level 2).**

With respect to the recommendation of first-line antibiotic intervention, as well as treatment duration/cessation, the consensus of the Delphi panel was as follows:

- **For early-stage CBP and CP/CPPS patients, offer a quinolone (eg, ciprofloxacin or ofloxacin) for four to six weeks as first-line therapy (Level 5).**

- **A repeated course of antibiotic therapy (of four to six weeks) should only be offered if a bacterial cause is confirmed or there is a history of repeated UTI (Level 5).**
- **If a bacterial cause is excluded (eg, via urine dipstick or urine culture analysis) and no patient symptom improvement is observed after antibiotic therapy, a different treatment modality or referral to specialist care should be considered (Level 5).**

Table 4. Antibiotic treatment options[a]

Antibiotic	Advantages	Considerations	PERG recommendation
Quinolones **e.g. CIPROFLOXACIN**	• Favourable pharmacokinetic profile • Excellent penetration into the prostate • Good bioavailability • Good activity against typical and atypical pathogens	Depending on substance: ▪ drug interactions ▪ phototoxicity ▪ central nervous system adverse events.	Consider: first-line Dose and duration should be sufficient to eradicate the infection, e.g. CIPROFLOXACIN 500 mg bd 28/7
TRIMETHOPRIM	• Active against most relevant pathogens • Monitoring unnecessary • Good penetration into the prostate	• No activity against *Pseudomonas*, some enterococci and some enterobacteriaceae	Consider: second-line Dose and duration should be sufficient to eradicate the infection, e.g. TRIMETHOPRIM 200 mg bd 28/7
Tetracyclines **e.g. DOXYCYCLINE**	• Good activity against *Chlamydia* and *Mycoplasma*	• Contraindicated in renal and liver failure • Unreliable activity against coagulase-negative staphylococci, E. coli, other enterobacteriaceae, and enterococci • No activity against *P. Aeruginosa* • Risk of skin sensitisation	Consider: second-line Dose and duration should be sufficient to eradicate the infection, e.g. DOXYCYCLINE 100 mg bd 28/7
Macrolides **e.g. AZITHROMYCIN**	• Good penetration into prostate • Active against *Chlamydia* and Gram-positive bacteria	• Minimal supporting data from randomised controlled trials • Unreliable activity against Gram-negative bacteria	Reserve for special indications, based on advice from microbiologist and microbiological findings

[a] Based on information adapted from Grabe *et al,* 2013[22], the British National Formulary[85] and PERG expert consensus. Abbreviations: bd = twice-daily; 28/7= seven days a week for four weeks.

Pain relief

Published evidence on the use of pharmacotherapy for pain relief in CBP and CP/CPPS populations is scarce. Only two RCTs were identified for non-steroidal anti-inflammatory drugs (NSAIDs), one of which evaluated rofecoxib,[86] which has now been withdrawn from the market. The second RCT evaluated celecoxib in CP/CPPS patients, which produced a statistically significant decrease in NIH-CPSI total ($p<0.015$), pain ($p<0.006$) and QoL ($p<0.032$) scores after two, four and six weeks; however, the effects were limited to the short duration of therapy.[87] A randomised comparative study (n=50) that evaluated ibuprofen versus a terpenic mixture (Rowatinex®) in CP/CPPS was also found; the patient cohort treated with ibuprofen (n=25) did show a significant improvement in total, pain and QoL NIH-CPSI scores after six weeks of treatment compared with baseline, but the terpene mixture outperformed ibuprofen.[88] However, the small size and lack of a placebo arm circumvents any strong conclusions from being drawn. The conclusions from two recent meta-analyses were mixed; one reported that NSAIDs were 80% more likely to achieve a favourable response than placebo (n=190, relative risk [RR]: 1.8; 95% confidence interval [CI]: 1.2–2.6), based on the combination of three trials evaluating rofecoxib, celecoxib and a corticosteroid.[71] The second analysis, based on only the rofecoxib and celecoxib trials, concluded that no significant differences in efficacy could be ascertained for NSAIDs versus placebo.[72]

No trials were identified that evaluated opioid analgesics in the CBP or CP/CPPS populations. For co-analgesics, only one RCT was identified, which evaluated pregabalin (n=218) versus placebo (n=106) in the CP/CPPS population.[12] Compared with the placebo group, the patients in the pregabalin arm experienced reductions in the NIH-CPSI total score and subscores ($p<0.05$). However, pregabalin therapy for six weeks was not superior to placebo in the rate of a six-point decrease in the NIH-CPSI total score, which is often classified as a clinically meaningful response, in men with CP/CPPS.[12] Due to the link between CP/CPPS and neuropathic pain,[3,11,12] guidance should be sought from the NICE clinical guideline on the pharmacological management of neuropathic pain[13] if a neuropathic pain state is suspected in CBP or CP/CPPS patients. The involvement of, or referral to, a specialist pain team should be sought in such cases.

Due to a lack of published RCT evidence for the use of pain relief medications in CBP and CP/CPPS populations, the Delphi panel approach was used to reach a consensus on what is considered to be best practice with respect to the treatment of pain symptoms in the initial or early stages of CBP and CP/CPPS. The consensus of the Delphi panel was as follows:

- **In patients with early-stage CBP and CP/CPPS who present with pain symptoms, regular paracetamol may be offered as analgesia (Level 5).**
- **NSAIDs should only be offered, for the short-term treatment of pain, to patients in the early stages of CBP and CP/CPPS, whose symptoms are suspected to be due to an inflammatory process, or those judged to be suffering the effects of an inflammatory flare, and they should be under regular review by a GP (Level 5).**

- **NSAIDs should be stopped within four to six weeks of treatment initiation if ineffective in reducing patient symptoms in order to prevent unwanted side effects (Level 5).**
- **In patients with early-stage CBP and CP/CPPS who present with pain symptoms, the use of opioids for pain relief should be avoided, due to the risk of opioid dependency (Level 5).**
- **If the route of patient pain is considered to be neuropathic in nature, treatment with a gabapentinoid (eg, pregabalin or gabapentin), a tricyclic antidepressant (eg, amitriptyline, nortriptyline or trimipramine) or a selective serotonin-norepinephrine[§] reuptake inhibitor (SNRI; eg, duloxetine) is warranted (Level 5).**

5-alpha-reductase inhibitors

The evidence-base for the use of 5-alpha-reductase inhibitors in CP/CPPS is limited, with only three small (n=41 to 76) RCTs identified, which evaluated finasteride.[89-91] The first RCT reported showed finasteride significantly reduces pain and voiding symptoms compared with baseline; however, no statistically significant differences compared with a small and non-comparable control group were observed, which was likely due to lack of power.[90] A later study, which compared finasteride with *Serenoa repens* (saw palmetto; a type of phytotherapy), showed that patients treated with finasteride had a significant and durable improvement (one-year trial duration) in NIH-CPSI total and pain domains, but not for urinary symptoms, when compared with baseline.[89] However, the trial size (n=64) and lack of a placebo arm are notable caveats. Nickel and colleagues showed better outcomes, via measurements of subjective overall assessment and NIH-CPSI scores, for finasteride versus placebo, but the results were not statistically significant.[91]

Although designed to assess whether dutasteride reduces the risk of prostate cancer in patients at increased risk (those aged 50–60 years and with PSA levels of >2.5 ng/ml or those over the age of 60 years with PSA levels >3.0 ng/ml), the REDUCE study prospectively examined the effect of dutasteride versus placebo in men with prostatitis-like pain (defined as NIH-CPSI pain subscore ≥5) and prostatitis-like syndrome (perineal or ejaculatory pain plus NIH-CPSI pain subscore ≥4) by evaluating NIH-CPSI scores at baseline and throughout the study (every six months for four years).[92] NIH-CPSI total score decreased significantly at 48 months in the dutasteride group versus placebo in men with prostatitis-like pain (n=678, p<0.0001) and with prostatitis-like syndrome (n=427, p=0.03). In addition, there were significantly more responders (defined as improvement of ≥4 units and ≥6 units in total CPSI score) with dutasteride versus placebo for both prostatitis subgroup populations assessed.[92] While the REDUCE study was not primarily designed as a CP/CPPS treatment trial, the significant reductions in NIH-CPSI scores compared with placebo in a relatively large patient cohort (n=1,105) with prostatitis-like pain or syndrome, suggests the use of 5-alpha-reductase inhibitors in older (aged ≥50 years) patients with PSA levels greater than 2.5 ng/ml (for those aged 50 to 60 years) or greater than 3.0 ng/ml (those aged >60 years) may be of clinical benefit; large, sufficiently powered RCTs, specifically in men with CP/CPPS, are needed to support this hypothesis.

[§] Known in the UK as noradrenaline

As described in the full NICE clinical guidelines for the management of LUTS in men,[30] a larger body of RCT evidence has evaluated the use of 5-alpha-reductase inhibitors to treat LUTS in men with BPE; such guidelines are signposted in **Appendix A.**

Based on the current published literature, the consensus treatment recommendation of the PERG was as follows:

- **There is insufficient evidence to warrant recommending 5-alpha-reductase inhibitors as a monotherapy approach in CP/CPPS, except for men who have co-existing BPE (Level 2).**

Combination/multimodal therapy

As discussed, patients with CBP or CP/CPPS can experience a number of different symptoms, typically across the pain, urinary, QoL and sexual dysfunction domains. Thus, the use of multiple interventions to target different symptom areas simultaneously may provide a more beneficial approach than monotherapy intervention.

The treatment combination evaluated the most within the literature has been that of alpha-blocker and antibiotic therapy. In a placebo-controlled trial, which compared tamsulosin versus ciprofloxacin versus their combination over six weeks in CP/CPPS patients, the total NIH-CPSI scores demonstrated significant mean improvement of approximately three to six points in all treatment groups from baseline. However, no statistically significant differences between treatment groups were observed.[61] Similar results were obtained in a comparison of doxazosin, levofloxacin and their combination, with the multimodal arm failing to provide any additional benefit over monotherapy.[93] However, small (n≤105) comparative trials evaluating combination therapies of tamsulosin plus levofloxacin[83] and doxazosin plus ciprofloxacin[84] have shown combination therapies outperformed monotherapy approaches in terms of NIH-CPSI score improvements. Assessment of tri- or quadmodal interventions evaluating mixtures of antibiotic, alpha-blocker, phytotherapy and/or physiotherapy techniques provide data in favour for combination therapies;[55,94,95] however, the lack of a comparison or placebo-controlled arm in these studies are notable caveats.

As described above, data available from head-to-head RCTs to conclusively support which multimodal/combination pharmacotherapy represents the best approach are limited, with trial data providing evidence both against and in support of multimodal/combination pharmacotherapy. The Delphi panel approach was, therefore, used to reach a consensus on what is considered to be best practice from expert experiences, and the panel concluded the following:

- **Multimodal/combination therapy should be uniquely designed for each individual patient, according to patient history, physical examination and evaluation testing (Level 5).**
- **In CBP and CP/CPPS patients, first-line multimodal/combination pharmacotherapy with an antibiotic plus an alpha-blocker may be considered as a treatment option, depending on the patient's symptoms at presentation (Level 5).**

- **In CBP and CP/CPPS patients, first-line multimodal/combination pharmacotherapy with an antibiotic plus an NSAID may be considered as a treatment option, depending on the patient's symptoms at presentation (Level 5).**
- **In CBP and CP/CPPS patients, multimodal/combination pharmacotherapy with an antibiotic plus an alpha-blocker plus an NSAID may be considered as a treatment option, depending on the patient's symptoms (Level 5).**
- **In CBP and CP/CPPS patients, multimodal/combination pharmacotherapy with an antibiotic plus an antineuropathic agent (eg, pregabalin) may be considered as a treatment option, depending on the patient's symptoms (Level 5).**
- **In CBP and CP/CPPS patients, multimodal/combination pharmacotherapy with an antibiotic plus a 5-alpha-reductase inhibitor may be considered as a treatment option, predominantly for patients with coexisting BPE (Level 5).**

Management recommendations – follow-up

Referral for specialist assessment and management

The PERG agreed that patients should be followed up at an interval of four to six weeks after their first presentation. No further action is required if symptoms have resolved. If a bacterial cause has been confirmed or the patient has had a partial response to antibiotics, a repeat course of antibiotic therapy should be considered. In these patients, as well as in those with persistent symptoms despite no identified bacterial cause and no response to antibiotics, the management should be guided by the symptoms present. In patients refractory to treatment, the consensus of the Delphi panel approach was as follows:

- **If a bacterial cause is excluded (eg, via urine dipstick or urine culture analysis) and no patient symptom improvement is observed after antibiotic therapy, a different treatment modality or referral to specialist care should be considered (Level 5).**
- **Patients who are refractory to treatment should be asked if they have a history of trauma (including physical, emotional or sexual abuse) in the past, including during childhood, since a proportion of patients may present with CP/CPPS-like symptoms due to previous trauma (Level 5).**[**]
- **Treatment of CBP and CP/CPPS patients requires input from a MDT, whereby the management with pharmacotherapy, physical and psychosocial approaches are integrated into a holistic treatment programme individualised for the patient (Level 5).**
- **The MDT responsible for the management of patients with CBP and CP/CPPS may include urologists, pain specialists, nurse specialists, physiotherapist, GPs, cognitive behavioural/psychological therapists and sexual health specialists (Level 5).**

Treatment strategies

Pain relief

As described in the recommendations for pain relief at initial presentation, RCT evidence for the use of pharmacotherapy approaches to treat pain in CBP and CP/CPPS populations is limited. If a neuropathic pain state is suspected, the involvement of a specialist pain team should be sought and the recommendations outlined in the NICE clinical guideline on the pharmacological management of neuropathic pain should be followed. Commonly used pharmacological treatments include antidepressants (tricyclic antidepressants and SNRIs), antiepileptic (anticonvulsant) drugs, topical treatments and opioid analgesics.[13] **Table 5** describes the dose and duration of

[**] Questions about abuse should only be implemented if the treating clinician has sufficient skills and resources to manage patients who have experienced abuse.

pharmacotherapy options that may be considered for the treatment of neuropathic pain. The consensus recommendation of the Delphi panel was as follows:

- **If the route of a patient's pain is considered to be neuropathic in nature, treatment with a gabapentinoid (eg, pregabalin or gabapentin), a tricyclic antidepressant (eg, amitriptyline, nortriptyline or trimipramine) or a selective serotonin-norepinephrine[††] reuptake inhibitor (eg, duloxetine) is warranted (Level 5).**

Patients may be, or become, treatment refractory to the pharmacotherapy approaches used to treat neuropathic pain. For these patients, the consensus recommendation of the PERG was as follows:

- **When a patient's pain is severe and refractory to the treatments outlined in Table 5, or when the pain is significantly impairing the patient's lifestyle and ability to participate in daily activities, the treating physician should consider referring the patient to a specialist pain service (Level 5).**

The role of the pain service is to provide a multidisciplinary assessment of the patient and to formulate a therapeutic management plan that combines treatment of the patient's pain, physical disability and psychosocial co-morbidity. Specialist treatments include:

- Surgical pain interventions; eg, nerve block procedures. In suitable patients, these can produce temporary or long-term pain relief and, in the context of a physical rehabilitation programme, can enable the patient to progress with physical therapy and rehabilitation
- Education and training in pain management strategies
- Optimisation of analgesic and antineuropathic medications
- Intensive and individualised specialist physical therapy or psychology
- Neuromodulation procedures, including spinal cord and sacral nerve root stimulation
- Some specialised pain services can provide physiotherapist- or psychologist-led pain management programmes for patients with poor physical function or complex pain problems.

With any pain condition, delay to recovery can lead to chronicity, a reduction in physical function and the development of psychosocial sequelae. Thus, early referral to a specialist pain service for patients who are not improving, despite appropriate treatment, is recommended.

[††] Known in the UK as noradrenaline

Table 5. Antineuropathic treatment options[a]

Analgesic class	Drug name	Starting dose	Maintenance dose	Common adverse effects	PERG practical points
Gabapentinoids	**GABAPENTIN**	100–300 mg at night	600 mg tds	Dizziness, sedation, dyspepsia, dry mouth, ataxia, peripheral oedema, weight gain.	Few drug interactions. Safe in overdose. Gut transport mechanism can become saturated limiting absorption from GI tract.
	PREGABALIN	50–75 mg at night	300 mg bd	Dizziness, sedation, dyspepsia, dry mouth, ataxia, peripheral oedema, weight gain.	Linear pharmacokinetics.
Tricyclic antidepressants/SNRIs	**AMITRIPTYLINE**	10 mg in evening	50–75 mg in evening	Sedation, dry mouth, blurred vision, urinary retention, constipation, postural hypotension, weight gain.	Many patients obtain pain relief at lower dose.
	DULOXETINE	30 mg in evening (or in morning, if insomnia)	60–120 mg od	Nausea, sedation, insomnia, headache, dizziness, dry mouth, constipation.	Less sedating. May cause insomnia in some patients.

[a] Based on information from the British National Formulary[85] and PERG expert consensus.
Abbreviations: bd = twice-daily; GI = gastrointestinal; od = once-daily; SNRIs = serotonin-norepinephrine reuptake inhibitors; tds = three times daily.

Specialist physiotherapy

Studies have shown that the symptoms of CBP and CP/CPPS may be the result of physical dysfunction, such as abnormal pelvic muscle spasm and muscle tenderness.[23,24] Thus, the use of physical techniques, in the form of specialist physiotherapy, may have a role in ameliorating symptoms of CBP and CP/CPPS.

Therapies that aim to improve relaxation and coordinated use of the pelvic floor muscles, such as biofeedback physical therapy and pelvic floor re-education, may also play a role in providing symptom improvement in CP/CPPS patients. Three small (n=19 to 31) pilot studies[96-98] have shown the introduction of a pelvic floor biofeedback re-educating programme significantly reduces symptom severity in patients with CP/CPPS. The largest of the three studies, which evaluated the effect of six to eight biofeedback sessions, demonstrated a mean reduction in the total NIH-CPSI score from 23.6 at baseline to 11.4 after treatment ($p<0.001$).[97] Neuromodulation by means of sacral nerve stimulation has also been reported to reduce pelvic pain with one sham-controlled medium-sized study (n=89) providing support for this; 12 weeks of percutaneous posterior tibial nerve stimulation produced significant improvement in the total NIH-CPSI score and visual analogue scale for pain in patients with non-inflammatory CP/CPPS.[99] Other small-to-medium studies suggest symptom improvement can be achieved by combining myofascial trigger point release with paradoxical relaxation training.[38,100,101] A small (n=24) randomised, placebo-controlled trial also provides support for the use of transcutaneous electrical nerve stimulation (TENS) in patients with CP/CPPS, with TENS demonstrating statistical significance over placebo with respect to a reduction in pain symptoms.[102]

Small pilot studies of acupuncture in CP/CPPS patients refractory to standard pharmacotherapy have provided positive results; in twelve men, the use of a six-week acupuncture regimen, (given twice weekly) achieved a significant decrease in total, pain, urinary and QoL NIH-CPSI scores after an average 33 weeks of follow-up ($p<0.05$).[103] Similarly, symptom improvements, as assessed by the NIH-CPSI, were seen with a five-week course[104] and six-week course[105] of acupuncture (on the bilateral BL33 region), with improvements pain, voiding symptoms and QoL in non-inflammatory CP/CPPS patients. Randomised, sham-controlled studies (n=39 to 89) support these results; a ten-week course of acupuncture proved almost twice as likely as sham treatment to improve CP/CPPS symptoms,[106] while a three-arm trial showed that after six weeks of electro-acupuncture, the NIH-CPSI total score had decreased significantly compared with the sham and advice and exercise groups alone ($p<0.001$).[107] A recent review of the evidence on the use of acupuncture in prostatitis concluded that the findings should encourage healthcare providers to apply acupuncture to manage pains of CP/CPPS, in conjunction with standard treatment.[108]

As described above, the majority of evidence for treating chronic forms of prostatitis with specialist physiotherapy is derived from small proof-of-principle or pilot studies, and little is reported on best practice approaches. The Delphi process, therefore, was used to reach a consensus about what is considered to be best practice with respect to physiotherapy as a treatment option for those with CP/CPPS. The consensus of the Delphi panel was as follows:

- **Before referral to specialist physiotherapy, a number of diagnostic tests (see Table 3) should be completed to confirm a physical causative route and to exclude non-physical causative routes for CBP and CP/CPPS symptoms, such as an STI screen, culture/microscopy of voided bladder urine, urethral smear, a *nucleic acid amplification test* and relevant pelvic physical examinations (Level 5).**
- **Once referred to physiotherapy, a full assessment (eg, symptom score scaling, examination of the pelvic floor muscles) should be completed to guide the subsequent pattern/order of physiotherapy treatment (Level 5).**
- **Once referred for physiotherapy, if a patient presents with psychosocial symptoms, a planned therapeutic strategy involving the introduction of stress management (including an explanation of the chronic pain cycle) should be considered in addition to seeking advice from the patient's GP or urologist with respect to potential onward referral to a psychosocial specialist (Level 5).**
- **The following specialist physiotherapy treatment options may be considered in CBP and CP/CPPS patients (Level 5):**
  - **Pelvic floor re-education**
  - **Local pelvic floor relaxation**
  - **Biofeedback**
  - **General relaxation**
  - **Deep relaxation/mindfulness**
  - **Trigger point release**
  - **Myofascial release**
  - **Stretches**
  - **Daily exercise encouraged for pain management**
  - **TENS**
  - **Acupuncture for trigger point release and pain management**
  - **Bladder retraining.**

It should be noted that the following specialist physiotherapy techniques for possible use in treating CBP and CP/CPPS were put to the Delphi panel, but a consensus on their suitability was not achieved:

- Core stability training
- Diaphragmatic breathing exercises
- Acupuncture for urgency and abdominal massage for constipation
- Defecation techniques.

However, these techniques may be suitable for certain patients and specialist physiotherapy should be a symptom-led approach.

Phytotherapy

Phytotherapy, which includes the use of pollen extracts, bioflavonoids and/or *Serenoa repens* (saw palmetto), is purported to have a relaxing effect on internal and external sphincter smooth muscles of the bladder and urethra, a strong anti-inflammatory effect, and an antiproliferative effect.[109] Three small RCTs were identified that evaluated the use of phytotherapy in the CP/CPPS population.[110-112] In a trial of a rye pollen extract (Cernilton) (n=70) versus placebo (n=69), the pollen extract significantly improved total, pain and QoL NIH-CPSI scores in patients with inflammatory CP/CPPS without severe side effects versus placebo.[112] Significant differences between another pollen extract (Prostat/Poltit) were demonstrated in a small (n=60) trial versus placebo, but a validated tool for symptom scoring was not used.[110] A small (n=30) RCT showed that the bioflavonoid quercetin, significantly improved clinical symptoms in CP/CPPS, as assessed by changes in NIH-CPSI scores versus placebo, with the improvement in total score stemming from improvements in the pain score (10.3 to 6.2, p=0.005) and QoL score (8 to 4.9, p=0.004) but not the urinary score (2.7 to 1.5, p=not significant).[111] A recent network meta-analysis of these trials indicated phytotherapy offers a favourable response rate over placebo (RR: 1.6; 95% CI: 1.1–2.4).[71]

A prospective, comparative trial provides additional evidence that phytotherapy offers symptom improvement in inflammatory CP/CPPS, with significant changes in symptoms from baseline observed for Profluss® (*Serenoa repens*, selenium, and lycopene).[113] However, CP/CPPS patients treated with *Serenoa repens* reported no appreciable long-term improvement in NIH-CPSI scores in a one-year comparative study against finasteride.[89] The only trial in the CBP population compared the addition of four phytotherapy agents (*Serenoa repens*, *U. dioica,* curcumin and quercetin) to antibiotic treatment versus antibiotic treatment alone; significant differences in favour of the combination treatment were observed.[114]

Based on the current published literature, the consensus treatment recommendations of the PERG was as follows:

- **Phytotherapy has a modest beneficial effect on symptom improvement in CBP and CP/CPPS and may be considered as a treatment option in treatment-refractory patients (Level 2).**

Cognitive behavioural therapy and psychotherapy

While it is recognised that psychosocial symptoms may be part of CBP and CP/CPPS,[32-35] no evidence from RCTs or comparative studies is available to support the use of psychological treatment or cognitive behavioural therapy (CBT). The Delphi process was used to reach a consensus about what is considered to be best practice with respect to CBT and psychotherapy.

The consensus of the Delphi panel was as follows:

- **Psychosocial symptoms should be assessed both in the early and late stages of CBP and CP/CPPS. If there is a significant suspicion of psychological factors contributing to a patient's condition, these should be screened for (Level 5).**
- **CBT should be considered in conjunction with other treatments in patients with later-stage CBP and CP/CPPS, as it may improve pain and QoL (Level 5).**

Surgical intervention

The evidence on surgical management techniques in the treatment of CBP or CP/CPPS, such as prostatectomy, transurethral resection of the prostate (TURP), transrectal high-intensity focused ultrasound (HIFU), or prostatic massage is very limited. Results of small (n<40) pilot studies suggested transurethral needle ablation[115] and transurethral microwave thermotherapy[116] offered some symptom improvement compared with baseline in CP/CPPS patients, but large RCTs are required before firm conclusions about the clinical effectiveness of such surgical interventions can be made.

A systematic review conducted in 2008 evaluated the clinical effectiveness of repetitive prostatic massage in treating CBP and CP/CPPS and identified four studies covering 195 patients, which included a randomised prospective study, two case series and an anecdotal report.[117] The largest study in this review evaluated two subgroups receiving either a combination of antibiotics and tri-weekly prostatic massage for one month (n=42) or antibiotics alone for the same period (n=39). Overall, a statistically significant reduction in the NIH-CPSI total and domain scores was observed after treatment. However, no difference was recorded between the post-treatment scores of patients who did or did not receive repeated prostatic massage.[118] The review concluded that the available studies do not provide high-quality evidence, due to the lack of randomised placebo/sham-controlled trials.[117] In addition, no two studies have used the same protocol or tool for outcome measurement, thus preventing the pooling of data.[117] The use of repetitive prostatic massage or prostatic massage under general anaesthetic as treatment options in refractory patients was put forward to the Delphi panel for comment and response; however, no consensus was reached on their potential use.

Based on the current published literature, the consensus treatment recommendation of the PERG was as follows:

- **There is insufficient evidence to warrant recommending surgical techniques, including radical prostatectomy, transurethral resection of the prostate, transrectal high-intensity focused ultrasound, or prostatic massage for the treatment of CBP or CP/CPPS, except in the context of a clinical trial setting (Level 3).**

Research recommendations

The consensus of the PERG was that current evidence is insufficient, and further research is required in the following areas:

- **In CP/CPPS patients who are refractory to initial mono-pharmacotherapy approaches, further research into multimodal pharmacotherapy is warranted. Randomised, placebo-controlled trials should be performed to establish pharmacotherapy treatment options for those who fail to show symptom responses to initial monotherapy treatment modalities.**

- **Further research is required to establish the clinical benefits of 5-alpha-reductase inhibitors, specifically in the CP/CPPS population, especially older (>50 years) patients and/or those at increased risk of prostate cancer (PSA levels >2.5 ng/ml in a man aged 50–60 years or 3.0 ng/ml in a man aged over 60 years).**

- **Further research is required to evaluate the cost impact and effectiveness of interventions to treat CBP and CPPS to help inform future cases for service redesign.**

- **Further research is required to assess the effectiveness of a multidisciplinary approach and symptom-based management over 'usual care' for CBP and CP/CPPS patients.**

- **Further research is required to assess the use of daily phosphodiesterase type 5 (PDE5) inhibitors for those with CBP or CP/CPPS plus sexual symptoms such as ED.**

- **Further research is required to assess the prevalence and impact of psychological factors in CBP and CP/CPPS patient. Research on the effectiveness of specific treatments, such as mindfulness/relaxation, would be useful in these patients groups.**

- **Further research is required to investigate the possible association of CBP and CP/CPPS with other co-morbidities; for example, IBS.**

- **Clinical studies and RCTs on any treatment modality for the management of CBP or CP/CPPS need to include long-term (at least five years) follow-up with annual assessments**.

Acknowledgements

The authors would like to acknowledge Fiona Carter, of South West Training Surgical Network, for providing consultancy services during the Delphi panel process by acting as a moderator during questionnaire round refinement. In addition, the authors would like to thank Hayward Medical Communications for providing writing and editorial support to develop the guideline. The authors would like to thank all Delphi panel members who participated in the process.

Updating the guideline

This guideline was issued in September 2014 and will be considered for review in September 2017, unless evidence updates within the area suggest otherwise. Any updates to the guideline will be noted on the Prostate Cancer UK website.

Conflicts of interest

Prostate Cancer UK funded the project and guideline development. The funding that Prostate Cancer UK receives from pharmaceutical and medical device companies does not exceed 5% of its total annual income. Such funding was not used for the development of this guideline. Hayward Medical Communications is a commercial organisation who received funding from Prostate Cancer UK to manage the literature review, web-based Delphi process and development of the guideline. All PERG members and Delphi panel members participated in the process on a voluntarily basis. Jon Rees (PERG chair) has done consultancy work for and received speaker fees from Prostate Cancer UK for providing GP medical education classes. All other PERG members declared no conflicts of interest.

Comments or feedback

Please submit any comments or feedback on the guideline to: evidence@prostatecanceruk.org

References

1. Krieger JN, Lee SW, Jeon J *et al*. Epidemiology of prostatitis. *Int J Antimicrob Agents* 2008; **31 Suppl 1:** S85-90.
2. Pavone-Macaluso M. Chronic Prostatitis Syndrome: A Common, but Poorly Understood Condition. Part I. *EAU-EBU Update Series* 2007; **5:** 1–15.
3. Engeler DS, Baranowski AP, Elneil S *et al*. *Guidelines on chronic pelvic pain*. European Association of Urology, 2012. www.uroweb.org/gls/pdf/24_Chronic_Pelvic_Pain_LR%20II.pdf (last accessed 06 June 2014)
4. Clemens JQ, Meenan RT, O'Keeffe Rosetti MC, Gao SY, Calhoun EA. Incidence and clinical characteristics of National Institutes of Health type III prostatitis in the community. *J Urol* 2005; **174:** 2319-2322.
5. Daniels NA, Link CL, Barry MJ, McKinlay JB. Association between past urinary tract infections and current symptoms suggestive of chronic prostatitis/chronic pelvic pain syndrome. *J Natl Med Assoc* 2007; **99:** 509-516.
6. Schaeffer AJ. Epidemiology and evaluation of chronic pelvic pain syndrome in men. *Int J Antimicrob Agents* 2008; **31 Suppl 1:** S108-111.
7. Mahal BA, Cohen JM, Allsop SA *et al*. The role of phenotyping in chronic prostatitis/chronic pelvic pain syndrome. *Curr Urol Rep* 2011; **12:** 297-303.
8. Zhao Z, Zhang J, He J, Zeng G. Clinical utility of the UPOINT phenotype system in Chinese males with chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS): a prospective study. *PLoS One* 2013; **8:** e52044.
9. Murphy AB, Macejko A, Taylor A, Nadler RB. Chronic prostatitis: management strategies. *Drugs* 2009; **69:** 71-84.
10. Wagenlehner FM, van Till JW, Magri V *et al*. National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) symptom evaluation in multinational cohorts of patients with chronic prostatitis/chronic pelvic pain syndrome. *Eur Urol* 2013; **63:** 953-959.
11. Aboumarzouk OM, Nelson RL. Pregabalin for chronic prostatitis. *Cochrane Database Syst Rev* 2012; **8:** CD009063.
12. Pontari MA, Krieger JN, Litwin MS *et al*. Pregabalin for the treatment of men with chronic prostatitis/chronic pelvic pain syndrome: a randomized controlled trial. *Arch Intern Med* 2010; **170:** 1586-1593.
13. National Institute for Health and Care Excellence. *Neuropathic pain – pharmacological management: The pharmacological management of neuropathic pain in adults in non-specialist settings. NICE CG 173*. NICE, 2013. www.nice.org.uk/guidance/cg173/resources/guidance-neuropathic-pain-pharmacological-management-pdf (last accessed 14 July 2014)
14. McNaughton Collins M, Pontari MA, O'Leary MP *et al*. Quality of life is impaired in men with chronic prostatitis: the Chronic Prostatitis Collaborative Research Network. *J Gen Intern Med* 2001; **16:** 656-662.
15. Nyberg LM, Krieger JN, Nickel JC. National Institutes of Health Classification of Chronic Prostatitis. In: Nickel JC (ed). *Textbook of Prostatitis*. London: CRC Press, 1999.
16. Lazaro N. *Sexually transmitted infections in primary care*. Royal College of General Practitioners, 2013. www.rcgp.org.uk/clinical-andresearch/clinical-resources/~/media/Files/CIRC/RCGP-Sexually-Transmitted-Infections-in-Primary-Care-2013.ashx (last accessed 06 June 2014)
17. NHS Choices. Map of Medicine. Prostatitis – Primary Care, January 2014. http://healthguides.mapofmedicine.com/choices/pdf/prostatitis1.pdf (last accessed 06 June 2014)
18. NHS Choices. Map of Medicine. Prostatitis – Secondary Care, January 2014. http://healthguides.mapofmedicine.com/choices/pdf/prostatitis2.pdf (last accessed 06 June 2014)
19. University of Oxford Centre for Evidence Based Medicine. OCEBM Levels of Evidence System. www.cebm.net/index.aspx?o=5653 (last accessed 06 June 2014)
20. Hsu CC, Sandford BA. The Delphi Technique: Making Sense of Consensus. *Practical Assessment, Research & Evaluation* 2007; **12:** 1–8.
21. Litwin MS, McNaughton-Collins M, Fowler FJ, Jr. *et al*. The National Institutes of Health chronic prostatitis symptom index: development and validation of a new outcome measure. Chronic Prostatitis Collaborative Research Network. *J Urol* 1999; **162:** 369-375.
22. Grabe M, Bjerklund-Johansen TE, Botto H *et al*. *Guidelines on urological infections*. European Association of Urology, 2013. www.uroweb.org/gls/pdf/18_Urological%20infections_LR.pdf (last accessed 06 June 2014)
23. Hetrick DC, Ciol MA, Rothman I *et al*. Musculoskeletal dysfunction in men with chronic pelvic pain syndrome type III: a case-control study. *J Urol* 2003; **170:** 828-831.

24. Shoskes DA, Berger R, Elmi A *et al*. Muscle tenderness in men with chronic prostatitis/chronic pelvic pain syndrome: the chronic prostatitis cohort study. *J Urol* 2008; **179:** 556-560.
25. Clemens JQ, Brown SO, Kozloff L, Calhoun EA. Predictors of symptom severity in patients with chronic prostatitis and interstitial cystitis. *J Urol* 2006; **175:** 963-966; discussion 967.
26. Vicari E, La Vignera S, Arcoria D *et al*. High frequency of chronic bacterial and non-inflammatory prostatitis in infertile patients with prostatitis syndrome plus irritable bowel syndrome. *PLoS One* 2011; **6:** e18647.
27. Vicari E, Calogero AE, Condorelli RA, Vicari LO, La Vignera S. Male accessory gland infection frequency in infertile patients with chronic microbial prostatitis and irritable bowel syndrome: transrectal ultrasound examination helps to understand the links. *J Androl* 2012; **33:** 404-411.
28. Nickel JC. The overlapping lower urinary tract symptoms of benign prostatic hyperplasia and prostatitis. *Curr Opin Urol* 2006; **16:** 5-10.
29. Bartoletti R, Cai T, Mondaini N *et al*. Prevalence, incidence estimation, risk factors and characterization of chronic prostatitis/chronic pelvic pain syndrome in urological hospital outpatients in Italy: results of a multicenter case-control observational study. *J Urol* 2007; **178:** 2411-2415; discussion 2415.
30. National Clinical Guideline Centre. *The Management of lower urinary tract symptoms in men. Methods, Evidence & Guidance*. NCGC, 2010. www.nice.org.uk/guidance/cg97/resources/cg97-lower-urinary-tract-symptoms-full-guideline3 (last accessed 14 July 2014)
31. Nickel JC. Classification and diagnosis of prostatitis: a gold standard? *Andrologia* 2003; **35:** 160-167.
32. Clemens JQ, Brown SO, Calhoun EA. Mental health diagnoses in patients with interstitial cystitis/painful bladder syndrome and chronic prostatitis/chronic pelvic pain syndrome: a case/control study. *J Urol* 2008; **180:** 1378-1382.
33. Anderson RU, Orenberg EK, Chan CA, Morey A, Flores V. Psychometric profiles and hypothalamic-pituitary-adrenal axis function in men with chronic prostatitis/chronic pelvic pain syndrome. *J Urol* 2008; **179:** 956-960.
34. Ku JH, Jeon YS, Kim ME, Lee NK, Park YH. Psychological problems in young men with chronic prostatitis-like symptoms. *Scand J Urol Nephrol* 2002; **36:** 296-301.
35. Smith KB, Pukall CF, Tripp DA, Nickel JC. Sexual and Relationship Functioning in Men with Chronic Prostatitis/Chronic Pelvic Pain Syndrome and Their Partners. *Arch Sex Behav* 2007; **36:** 301–311.
36. Hedelin H. The chronic prostatitis/chronic pelvic pain syndrome and pain catastrophizing: a vicious combination. *Scand J Urol Nephrol* 2012; **46:** 273-278.
37. Sadeghi-Nejad H, Seftel A. Sexual dysfunction and prostatitis. *Curr Urol Rep* 2006; **7:** 479-484.
38. Anderson RU, Wise D, Sawyer T, Chan CA. Sexual dysfunction in men with chronic prostatitis/chronic pelvic pain syndrome: improvement after trigger point release and paradoxical relaxation training. *J Urol* 2006; **176:** 1534-1538; discussion 1538-1539.
39. Muller A, Mulhall JP. Sexual dysfunction in the patient with prostatitis. *Curr Opin Urol* 2005; **15:** 404–409.
40. Gonen M, Kalkan M, Cenker A, Ozkardes H. Prevalence of premature ejaculation in Turkish men with chronic pelvic pain syndrome. *J Androl* 2005; **26:** 601-603.
41. Mehta A, Stember DS, O'Brien K, Mulhall JP. Defining the aetiology of erectile dysfunction in men with chronic pelvic pain syndrome. *Andrology* 2013; **1:** 483-486.
42. Davis SN, Binik YM, Amsel R, Carrier S. Is a sexual dysfunction domain important for quality of life in men with urological chronic pelvic pain syndrome? Signs "UPOINT" to yes. *J Urol* 2013; **189:** 146-151.
43. Shoskes DA, Landis JR, Wang Y *et al*. Impact of post-ejaculatory pain in men with category III chronic prostatitis/chronic pelvic pain syndrome. *J Urol* 2004; **172:** 542-547.
44. Wagenlehner F, Pilatz A, Linn T *et al*. Prostatitis and andrological implications. *Minerva Urol Nefrol* 2013; **65:** 117-123.
45. Lee SW, Liong ML, Yuen KH *et al*. Adverse impact of sexual dysfunction in chronic prostatitis/chronic pelvic pain syndrome. *Urology* 2008; **71:** 79-84.
46. Magri V, Perletti G, Montanari E *et al*. Chronic prostatitis and erectile dysfunction: results from a cross-sectional study. *Arch Ital Urol Androl* 2008; **80:** 172-175.
47. Trinchieri A, Magri V, Cariani L *et al*. Prevalence of sexual dysfunction in men with chronic prostatitis/chronic pelvic pain syndrome. *Arch Ital Urol Androl* 2007; **79:** 67-70.
48. Liang CZ, Zhang XJ, Hao ZY, Shi HQ, Wang KX. Prevalence of sexual dysfunction in Chinese men with chronic prostatitis. *BJU Int* 2004; **93:** 568-570.

49. Davis SN, Morin M, Binik YM, Khalife S, Carrier S. Use of pelvic floor ultrasound to assess pelvic floor muscle function in Urological Chronic Pelvic Pain Syndrome in men. *J Sex Med* 2011; **8:** 3173-3180.
50. Liang CZ, Hao ZY, Li HJ *et al*. Prevalence of premature ejaculation and its correlation with chronic prostatitis in Chinese men. *Urology* 2010; **76:** 962-966.
51. Samplaski MK, Li J, Shoskes DA. Inclusion of erectile domain to UPOINT phenotype does not improve correlation with symptom severity in men with chronic prostatitis/chronic pelvic pain syndrome. *Urology* 2011; **78:** 653-658.
52. Nickel JC, Shoskes D, Wang Y *et al*. How does the pre-massage and post-massage 2-glass test compare to the Meares-Stamey 4-glass test in men with chronic prostatitis/chronic pelvic pain syndrome? *J Urol* 2006; **176:** 119-124.
53. Shoskes DA, Nickel JC, Rackley RR, Pontari MA. Clinical phenotyping in chronic prostatitis/chronic pelvic pain syndrome and interstitial cystitis: a management strategy for urologic chronic pelvic pain syndromes. *Prostate Cancer Prostatic Dis* 2009; **12:** 177-183.
54. Hedelin HH. Evaluation of a modification of the UPOINT clinical phenotype system for the chronic pelvic pain syndrome. *Scand J Urol Nephrol* 2009; **43:** 373-376.
55. Shoskes DA, Nickel JC, Kattan MW. Phenotypically directed multimodal therapy for chronic prostatitis/chronic pelvic pain syndrome: a prospective study using UPOINT. *Urology* 2010; **75:** 1249-1253.
56. Hu JC, Link CL, McNaughton-Collins M, Barry MJ, McKinlay JB. The association of abuse and symptoms suggestive of chronic prostatitis/chronic pelvic pain syndrome: results from the Boston Area Community Health survey. *J Gen Intern Med* 2007; **22:** 1532-1537.
57. Weidner W, Anderson RU. Evaluation of acute and chronic bacterial prostatitis and diagnostic management of chronic prostatitis/chronic pelvic pain syndrome with special reference to infection/inflammation. *Int J Antimicrob Agents* 2008; **31 Suppl 1:** S91-95.
58. Magri V, Cariani L, Bonamore R *et al*. Microscopic and microbiological findings for evaluation of chronic prostatitis. *Arch Ital Urol Androl* 2005; **77:** 135-138.
59. Nickel JC, Downey J, Clark J *et al*. Levofloxacin for chronic prostatitis/chronic pelvic pain syndrome in men: a randomized placebo-controlled multicenter trial. *Urology* 2003; **62:** 614-617.
60. Burford D, Kirby M, Austoker J. *Prostate Cancer Risk Management Programme information for primary care; PSA testing in asymptomatic men. Evidence document*. NHS Cancer Screening Programmes, 2010. www.cancerscreening.nhs.uk/prostate/pcrmp02.pdf (last accessed 07 July 2014)
61. Alexander RB, Propert KJ, Schaeffer AJ *et al*. Ciprofloxacin or tamsulosin in men with chronic prostatitis/chronic pelvic pain syndrome: a randomized, double-blind trial. *Ann Intern Med* 2004; **141:** 581-589.
62. Chen Y, Wu X, Liu J *et al*. Effects of a 6-month course of tamsulosin for chronic prostatitis/chronic pelvic pain syndrome: a multicenter, randomized trial. *World J Urol* 2011; **29:** 381-385.
63. Nickel JC, Narayan P, McKay J, Doyle C. Treatment of chronic prostatitis/chronic pelvic pain syndrome with tamsulosin: a randomized double blind trial. *J Urol* 2004; **171:** 1594-1597.
64. Mehik A, Alas P, Nickel JC, Sarpola A, Helstrom PJ. Alfuzosin treatment for chronic prostatitis/chronic pelvic pain syndrome: a prospective, randomized, double-blind, placebo-controlled, pilot study. *Urology* 2003; **62:** 425-429.
65. Nickel JC, Krieger JN, McNaughton-Collins M *et al*. Alfuzosin and symptoms of chronic prostatitis-chronic pelvic pain syndrome. *N Engl J Med* 2008; **359:** 2663-2673.
66. Evliyaoglu Y, Burgut R. Lower urinary tract symptoms, pain and quality of life assessment in chronic non-bacterial prostatitis patients treated with alpha-blocking agent doxazosin; versus placebo. *Int Urol Nephrol* 2002; **34:** 351-356.
67. Tugcu V, Tasci AI, Fazlioglu A *et al*. A placebo-controlled comparison of the efficiency of triple- and monotherapy in category III B chronic pelvic pain syndrome (CPPS). *Eur Urol* 2007; **51:** 1113-1117; discussion 1118.
68. Cheah PY, Liong ML, Yuen KH *et al*. Initial, long-term, and durable responses to terazosin, placebo, or other therapies for chronic prostatitis/chronic pelvic pain syndrome. *Urology* 2004; **64:** 881-886.
69. Gul O, Eroglu M, Ozok U. Use of terazosine in patients with chronic pelvic pain syndrome and evaluation by prostatitis symptom score index. *Int Urol Nephrol* 2001; **32:** 433-436.
70. Nickel JC, O'Leary MP, Lepor H *et al*. Silodosin for men with chronic prostatitis/chronic pelvic pain syndrome: results of a phase II multicenter, double-blind, placebo controlled study. *J Urol* 2011; **186:** 125-131.
71. Anothaisintawee T, Attia J, Nickel JC *et al*. Management of chronic prostatitis/chronic pelvic pain syndrome: a systematic review and network meta-analysis. *JAMA* 2011; **305:** 78-86.
72. Cohen JM, Fagin AP, Hariton E *et al*. Therapeutic intervention for chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS): a systematic review and meta-analysis. *PLoS One* 2012; **7:** e41941.

73. Magri V, Marras E, Skerk V *et al*. Eradication of Chlamydia trachomatis parallels symptom regression in chronic bacterial prostatitis patients treated with a fluoroquinolone-macrolide combination. *Andrologia* 2010; **42:** 366-375.
74. Nickel JC, Xiang J. Clinical significance of nontraditional bacterial uropathogens in the management of chronic prostatitis. *J Urol* 2008; **179:** 1391-1395.
75. Skerk V, Krhen I, Lisic M *et al*. Comparative randomized pilot study of azithromycin and doxycycline efficacy in the treatment of prostate infection caused by Chlamydia trachomatis. *Int J Antimicrob Agents* 2004; **24:** 188-191.
76. Skerk V, Schonwald S, Krhen I *et al*. Comparative analysis of azithromycin and ciprofloxacin in the treatment of chronic prostatitis caused by Chlamydia trachomatis. *Int J Antimicrob Agents* 2003; **21:** 457-462.
77. Skerk V, Schonwald S, Krhen I *et al*. Comparative analysis of azithromycin and clarithromycin efficacy and tolerability in the treatment of chronic prostatitis caused by Chlamydia trachomatis. *J Chemother* 2002; **14:** 384-389.
78. Magri V, Trinchieri A, Ceriani I, Marras E, Perletti G. Eradication of unusual pathogens by combination pharmacological therapy is paralleled by improvement of signs and symptoms of chronic prostatitis syndrome. *Arch Ital Urol Androl* 2007; **79:** 93-98.
79. Bundrick W, Heron SP, Ray P *et al*. Levofloxacin versus ciprofloxacin in the treatment of chronic bacterial prostatitis: a randomized double-blind multicenter study. *Urology* 2003; **62:** 537-541.
80. Zhang ZC, Jin FS, Liu DM *et al*. Safety and efficacy of levofloxacin versus ciprofloxacin for the treatment of chronic bacterial prostatitis in Chinese patients. *Asian J Androl* 2012; **14:** 870-874.
81. Magri V, Montanari E, Skerk V *et al*. Fluoroquinolone-macrolide combination therapy for chronic bacterial prostatitis: retrospective analysis of pathogen eradication rates, inflammatory findings and sexual dysfunction. *Asian J Androl* 2011; **13:** 819-827.
82. Zhou Z, Hong L, Shen X *et al*. Detection of nanobacteria infection in type III prostatitis. *Urology* 2008; **71:** 1091-1095.
83. Ye ZQ, Lan RZ, Yang WM, Yao LF, Yu X. Tamsulosin treatment of chronic non-bacterial prostatitis. *J Int Med Res* 2008; **36:** 244-252.
84. Kulovac B, Aganovic D, Prcic A, Hadziosmanovic O. Management of chronic nonbacterial prostatitis/chronic pelvic pain syndrome. *Bosn J Basic Med Sci* 2007; **7:** 245-249.
85. *British National Formulary* 2014; **67**.
86. Nickel JC, Pontari M, Moon T *et al*. A randomized, placebo controlled, multicenter study to evaluate the safety and efficacy of rofecoxib in the treatment of chronic nonbacterial prostatitis. *J Urol* 2003; **169:** 1401-1405.
87. Zhao WP, Zhang ZG, Li XD *et al*. Celecoxib reduces symptoms in men with difficult chronic pelvic pain syndrome (Category IIIA). *Braz J Med Biol Res* 2009; **42:** 963-967.
88. Lee CB, Ha US, Lee SJ, Kim SW, Cho YH. Preliminary experience with a terpene mixture versus ibuprofen for treatment of category III chronic prostatitis/chronic pelvic pain syndrome. *World J Urol* 2006; **24:** 55-60.
89. Kaplan SA, Volpe MA, Te AE. A prospective, 1-year trial using saw palmetto versus finasteride in the treatment of category III prostatitis/chronic pelvic pain syndrome. *J Urol* 2004; **171:** 284-288.
90. Leskinen M, Lukkarinen O, Marttila T. Effects of finasteride in patients with inflammatory chronic pelvic pain syndrome: a double-blind, placebo-controlled, pilot study. *Urology* 1999; **53:** 502-505.
91. Nickel JC, Downey J, Pontari MA, Shoskes DA, Zeitlin SI. A randomized placebo-controlled multicentre study to evaluate the safety and efficacy of finasteride for male chronic pelvic pain syndrome (category IIIA chronic nonbacterial prostatitis). *BJU Int* 2004; **93:** 991-995.
92. Nickel JC, Roehrborn C, Montorsi F, Wilson TH, Rittmaster RS. Dutasteride reduces prostatitis symptoms compared with placebo in men enrolled in the REDUCE study. *J Urol* 2011; **186:** 1313-1318.
93. Jeong CW, Lim DJ, Son H, Lee SE, Jeong H. Treatment for chronic prostatitis/chronic pelvic pain syndrome: levofloxacin, doxazosin and their combination. *Urol Int* 2008; **80:** 157-161.
94. Magri V, Trinchieri A, Pozzi G *et al*. Efficacy of repeated cycles of combination therapy for the eradication of infecting organisms in chronic bacterial prostatitis. *Int J Antimicrob Agents* 2007; **29:** 549-556.
95. Shoskes DA, Hakim L, Ghoniem G, Jackson CL. Long-term results of multimodal therapy for chronic prostatitis/chronic pelvic pain syndrome. *J Urol* 2003; **169:** 1406-1410.
96. Clemens JQ, Nadler RB, Schaeffer AJ *et al*. Biofeedback, pelvic floor re-education, and bladder training for male chronic pelvic pain syndrome. *Urology* 2000; **56:** 951-955.
97. Cornel EB, van Haarst EP, Schaarsberg RW, Geels J. The effect of biofeedback physical therapy in men with Chronic Pelvic Pain Syndrome Type III. *Eur Urol* 2005; **47:** 607-611.

98. He W, Chen M, Zu X *et al*. Chronic prostatitis presenting with dysfunctional voiding and effects of pelvic floor biofeedback treatment. *BJU Int* 2010; **105:** 975-977.
99. Kabay S, Kabay SC, Yucel M, Ozden H. Efficiency of posterior tibial nerve stimulation in category IIIB chronic prostatitis/chronic pelvic pain: a Sham-Controlled Comparative Study. *Urol Int* 2009; **83:** 33-38.
100. Anderson RU, Wise D, Sawyer T, Chan C. Integration of myofascial trigger point release and paradoxical relaxation training treatment of chronic pelvic pain in men. *J Urol* 2005; **174:** 155-160.
101. Anderson RU, Wise D, Sawyer T, Glowe P, Orenberg EK. 6-day intensive treatment protocol for refractory chronic prostatitis/chronic pelvic pain syndrome using myofascial release and paradoxical relaxation training. *J Urol* 2011; **185:** 1294-1299.
102. Sikiru L, Shmaila H, Muhammed SA. Transcutaneous electrical nerve stimulation (TENS) in the symptomatic management of chronic prostatitis/chronic pelvic pain syndrome: a placebo-control randomized trial. *Int Braz J Urol* 2008; **34:** 708-713; discussion 714.
103. Chen R, Nickel JC. Acupuncture ameliorates symptoms in men with chronic prostatitis/chronic pelvic pain syndrome. *Urology* 2003; **61:** 1156-1159; discussion 1159.
104. Honjo H, Kamoi K, Naya Y *et al*. Effects of acupuncture for chronic pelvic pain syndrome with intrapelvic venous congestion: preliminary results. *Int J Urol* 2004; **11:** 607-612.
105. Tugcu V, Tas S, Eren G *et al*. Effectiveness of acupuncture in patients with category IIIB chronic pelvic pain syndrome: a report of 97 patients. *Pain Med* 2010; **11:** 518-523.
106. Lee SW, Liong ML, Yuen KH *et al*. Acupuncture versus sham acupuncture for chronic prostatitis/chronic pelvic pain. *Am J Med* 2008; **121:** 79 e71-77.
107. Lee SH, Lee BC. Electroacupuncture relieves pain in men with chronic prostatitis/chronic pelvic pain syndrome: three-arm randomized trial. *Urology* 2009; **73:** 1036-1041.
108. Lee SH, Lee BC. Use of acupuncture as a treatment method for chronic prostatitis/chronic pelvic pain syndromes. *Curr Urol Rep* 2011; **12:** 288-296.
109. Wagenlehner FM, Bschleipfer T, Pilatz A, Weidner W. Pollen extract for chronic prostatitis-chronic pelvic pain syndrome. *Urol Clin North Am* 2011; **38:** 285-292.
110. Elist J. Effects of pollen extract preparation Prostat/Poltit on lower urinary tract symptoms in patients with chronic nonbacterial prostatitis/chronic pelvic pain syndrome: a randomized, double-blind, placebo-controlled study. *Urology* 2006; **67:** 60-63.
111. Shoskes DA, Zeitlin SI, Shahed A, Rajfer J. Quercetin in men with category III chronic prostatitis: a preliminary prospective, double-blind, placebo-controlled trial. *Urology* 1999; **54:** 960-963.
112. Wagenlehner FM, Schneider H, Ludwig M *et al*. A pollen extract (Cernilton) in patients with inflammatory chronic prostatitis-chronic pelvic pain syndrome: a multicentre, randomised, prospective, double-blind, placebo-controlled phase 3 study. *Eur Urol* 2009; **56:** 544-551.
113. Morgia G, Mucciardi G, Gali A *et al*. Treatment of chronic prostatitis/chronic pelvic pain syndrome category IIIA with Serenoa repens plus selenium and lycopene (Profluss) versus S. repens alone: an Italian randomized multicenter-controlled study. *Urol Int* 2010; **84:** 400-406.
114. Cai T, Mazzoli S, Bechi A *et al*. Serenoa repens associated with Urtica dioica (ProstaMEV) and curcumin and quercitin (FlogMEV) extracts are able to improve the efficacy of prulifloxacin in bacterial prostatitis patients: results from a prospective randomised study. *Int J Antimicrob Agents* 2009; **33:** 549-553.
115. Chiang PH, Chiang CP. Therapeutic effect of transurethral needle ablation in non-bacterial prostatitis: chronic pelvic pain syndrome type IIIa. *Int J Urol* 2004; **11:** 97-102.
116. Kastner C, Hochreiter W, Huidobro C, Cabezas J, Miller P. Cooled transurethral microwave thermotherapy for intractable chronic prostatitis--results of a pilot study after 1 year. *Urology* 2004; **64:** 1149-1154.
117. Mishra VC, Browne J, Emberton M. Role of repeated prostatic massage in chronic prostatitis: a systematic review of the literature. *Urology* 2008; **72:** 731-735.
118. Ateya A, Fayez A, Hani R *et al*. Evaluation of prostatic massage in treatment of chronic prostatitis. *Urology* 2006; **67:** 674-678.

Appendices

A ***Relevant supporting information***

B ***Prostatitis Expert Reference Group Members***

Supplementary Appendices

1 ***Literature review protocol***

Appendix A – Relevant supporting information

1. **Guidelines on chronic pelvic pain. European Association of Urology; 2012.**
   Engeler DS, Baranowski AP, S. Elneil, et al.
   Available from: http://www.uroweb.org/gls/pdf/24_Chronic_Pelvic_Pain_LR%20II.pdf

2. **Guidelines on urological infections. European Association of Urology; 2013**. Grabe M, Bjerklund-Johansen TE, Botto H et al.
   Available from: http://www.uroweb.org/gls/pdf/18_Urological%20infections_LR.pdf

3. **NHS Choices; Map of Medicine. Prostatitis – Primary Care; January 2014**.
   Available from: http://healthguides.mapofmedicine.com/choices/pdf/prostatitis1.pdf

4. **NHS Choices; Map of Medicine. Prostatitis – Secondary Care, January 2014.** Available from: http://healthguides.mapofmedicine.com/choices/pdf/prostatitis2.pdf

5. **National Institute for Health and Care Excellence Clinical Guideline 97 – Lower urinary tract symptoms; May 2010**
   Available from: http://www.nice.org.uk/guidance/cg97/resources/guidance-lower-urinary-tract-symptoms-pdf

6. **National Institute for Health and Care Excellence Clinical Guideline 97 – Lower urinary tract symptoms; FULL GUIDELINE; May 2010**
   Available from: http://www.nice.org.uk/guidance/cg97/resources/cg97-lower-urinary-tract-symptoms-full-guideline3

7. **National Institute for Health and Care Excellence Clinical Guideline 173 - Neuropathic pain – pharmacological management; November 2013**
   Available from: http://www.nice.org.uk/guidance/cg173/resources/guidance-neuropathic-pain-pharmacological-management-pdf

8. **Sexually transmitted infections in primary care. Royal College of General Practitioners/British Association for Sexual Health and HIV; 2013.**
   Lazaro, N
   Available from: http://www.rcgp.org.uk/clinical-andresearch/clinical-resources/~/media/Files/CIRC/RCGP-Sexually-Transmitted-Infections-in-Primary-Care-2013.ashx

9. **National Institute for Health and Care Excellence Clinical Guideline 90 – the treatment and management of depression in adults; October 2009**
   Available from: http://www.nice.org.uk/guidance/cg90/resources/guidance-depression-in-adults-pdf

10. **National Institute for Health and Care Excellence Clinical Guideline 91 – Depression in adults with a chronic physical health problem; October 2009**
    Available from: http://www.nice.org.uk/guidance/cg91/resources/guidance-depression-in-adults-with-a-chronic-physical-health-problem-pdf

11. **Prostatitis: A guide to infection or inflammation of the prostate**
    Available from: http://prostatecanceruk.org/media/41604/prostatitis.pdf

12. **British Society of Sexual Medicine Guidelines on the management of Erectile Dysfunction (2013 edition)**
    Available from: http://www.bssm.org.uk/downloads/BSSM_ED_Management_Guidelines_2013.pdf

Appendix B – Prostatitis Expert Reference Group Members

Jon Rees (Chair)

General Practitioner, Backwell and Nailsea Medical Group, Bristol

Mark Abrahams

Pain Consultant, Addenbrooke's Hospital, Cambridge

Victor Abu

Clinical Nurse Specialist – Prostate, University College London Hospitals, London

Trevor Allan

Patient Representative

Andrew Doble

Consultant Urologist, Addenbrooke's Hospital, Cambridge

Theresa Neale

Urology Clinical Nurse Specialist, South Warwickshire Foundation Trust

Penny Nixon

Physiotherapist Specialist, Addenbrooke's Hospital, Cambridge

Maxwell Saxty

Cognitive Behavioural Therapist, Addenbrooke's Hospital, Cambridge

Sarah Mee

Policy and Evidence Manager, Prostate Cancer UK, London

Alison Cooper

Senior Research Analyst, Prostate Cancer UK, London

Kirsty Haves

Senior Account Manager, Hayward Medical Communications, Newmarket

Jenny Lee

Project Manager, Hayward Medical Communications, Newmarket

Supplementary Appendix I – Literature review protocol

Medical Subject Headings (MeSH)

MeSH terms

The Medical Subject Headings (MeSH) terms were used within the search strategy to allow any studies indexed with the specified MeSH term to be identified. The exploded forms of MeSH terms were used to identify studies indexed with either the specified MeSH term itself or any of the more specific MeSH terms that fall below it in the MeSH tree structure.

MeSH subheadings

MeSH subheadings were combined with MeSH terms to identify relevant studies. For example, to find studies that report on the diagnosis of prostatitis, the following MeSH term and MeSH subheading were combined as a search term: exp Prostatitis/diagnosis.

Free text terms

In addition to the use of MeSH terms, free text searches of studies' titles and/or abstracts were used; for example: (prostatitis [Title/Abstract] AND syndrome[Title/Abstract]).

Filters applied

- Date threshold;
    - Studies published from 1 January 1999[7] – present [7 February 2014]
- Species;
    - Human (*Homo sapiens*)
- Languages;
    - English only
- Study type;
    - Clinical trials
    - Randomised control trials (RCTs)
    - Guidelines
    - Systematic Reviews

[7] The year of 1999 was chosen for the literature search as this was when clinical trials started reporting patients' symptoms using the validated National Institutes of Health Chronic Prostatitis Symptom Index tool

- Meta-analyses
- Observational studies

Inclusion/exclusion criteria

Although not applied through the use of formal filters, the following inclusion/exclusion criteria were applied manually during abstract screening and full text interrogation:

- Only studies evaluating adult (≥18 years old) males were included; ie, reports on female subjects and/or children were excluded
- Studies with <10 patients per arm were excluded
- Opinion articles/case reports were excluded
- Studies were excluded if the patient population fell under the NIH classification categories I (acute bacterial prostatitis) and IV (asymptomatic inflammatory prostatitis)
- Intervention studies were included if one of the following outcomes were measured:
  - NIH Chronic Prostatitis Symptom Index (NIH-CPSI)
  - International Index of Erectile Function-5 (IIEF-5)
  - International Prostate Symptom Score (IPSS)
  - Prostate Symptom Score Index (PSSI)
  - Hospital Anxiety and Depression Scale (HADS)
  - Patient Health Questionnaire-9 (PHQ-9)
  - Patient Health Questionnaire-2 (*PHQ-2*)
  - *Generalized Anxiety Disorder 7 (GAD-7)*
  - Subjective Overall Assessment (SOA*)*

Search strategy overview

The formal search strategy is described below. The following concepts were accounted for:

- Concept 1 (#1): CBP and CP/CPPS populations
- Concept 2 (#2): Diagnosis and assessment
- Concept 3 (#3): Sign and symptoms
- Concept 4 (#4): Treatment – Antibiotics
- Concept 5 (#5): Treatment – Non-steroidal anti-inflammatory agents
- Concept 6 (#6): Treatment – Analgesics
- Concept 7 (#7): Treatment – Alpha-blockers
- Concept 8 (#8): Treatment – 5-alpha-reductase inhibitors

- Concept 9 (#9): Treatment – Alternative therapies
- Concept 10 (#10): Treatment – Surgical intervention

Concepts 2 – 10 (inclusive) are each combined with Concept 1:

#1 AND (#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10)

Search strategy terms

Concept	Search string	N° of references
#1	Search **(((prostatitis[MeSH Terms]) OR pelvic pain[MeSH Terms])) AND ((chronic[Title/Abstract] AND prostatitis[Title/Abstract]) OR (prostatitis[Title/Abstract] AND syndrome[Title/Abstract]) OR (chronic[Title/Abstract] AND pelvic[Title/Abstract] AND pain[Title/Abstract]))** Filters: **Publication date from 1999/01/01 to 2014/02/07; Humans; English**	1573
#2	Search **((((("prostatitis/diagnosis"[Mesh Terms]) OR "pelvic pain/diagnosis"[Mesh Terms]) AND ("1999/01/01"[PDat] : "2014/02/07"[PDat]) AND Humans[Mesh] AND English[lang])) AND ((((((((((((((((((((((prostate[Title/Abstract] AND specific[Title/Abstract] AND antigen[Title/Abstract])) OR PSA[Title/Abstract]) OR (urine[Title/Abstract] AND analysis[Title/Abstract])) OR (digital[Title/Abstract] AND rectal[Title/Abstract] AND examination[Title/Abstract])) OR DRE[Title/Abstract]) OR (hypertonicity[Title/Abstract] AND pelvic[Title/Abstract] AND muscles[Title/Abstract])) OR (hypotonicity[Title/Abstract] AND pelvic[Title/Abstract] AND muscles[Title/Abstract])) OR (simplified[Title/Abstract] AND Meares-Stamey[Title/Abstract])) OR (simplified[Title/Abstract] AND Meares[Title/Abstract] AND Stamey[Title/Abstract])) OR ((microscopic[Title/Abstract] OR microscopy[Title/Abstract]) AND prostatic[Title/Abstract] AND fluid[Title/Abstract])) OR ((chlamydia[Title/Abstract] OR ureaplasma[Title/Abstract]) AND organisms[Title/Abstract])) OR (sperm[Title/Abstract] AND culture[Title/Abstract])) OR (anxiety[Title/Abstract] OR stress[Title/Abstract] OR depression[Title/Abstract])) OR (hospital[Title/Abstract] AND anxiety[Title/Abstract] AND depression[Title/Abstract] AND scale[Title/Abstract])) OR HADS[Title/Abstract]) OR (patient[Title/Abstract] AND health[Title/Abstract] AND questionnaire[Title/Abstract])) OR PHQ-9[Title/Abstract]) OR PHQ-2[Title/Abstract]) OR ((generalised[Title/Abstract] OR generalized[Title/Abstract]) AND anxiety[Title/Abstract] AND disorder[Title/Abstract] AND scale[Title/Abstract])) OR (GAD-7[Title/Abstract] OR GAD-2[Title/Abstract] OR UPOINT[Title/Abstract])) AND ("1999/01/01"[PDat] : "2014/02/07"[PDat]) AND Humans[Mesh] AND English[lang])** Filters: **Publication date from 1999/01/01 to 2014/02/07; Humans; English**	192
#1 AND #2		86
#3	Search **(lower[Title/Abstract] AND urinary[Title/Abstract] AND tract[Title/Abstract] AND symptoms[Title/Abstract]) OR (LUTS[Title/Abstract]) OR (overactive[Title/Abstract] AND bladder[Title/Abstract]) OR (urethral[Title/Abstract] AND burning[Title/Abstract]) OR (micturition[Title/Abstract]) OR (suprapubic[Title/Abstract] AND (pain[Title/Abstract] OR discomfort[Title/Abstract])) OR (erectile[Title/Abstract] AND dysfunction[Title/Abstract]) OR (pain[Title/Abstract] AND ejaculation[Title/Abstract]) OR ((pain[Title/Abstract] OR discomfort[Title/Abstract]) AND (inguinal[Title/Abstract] OR rectal[Title/Abstract] OR penile[Title/Abstract] OR perineal[Title/Abstract] OR lumbar[Title/Abstract] OR abdominal[Title/Abstract])) OR (haematospermia[Title/Abstract] OR hematospermia[Title/Abstract]) OR ((irritable[Title/Abstract] AND bowel[Title/Abstract] AND syndrome[Title/Abstract]) OR IBS[Title/Abstract]) OR (pelvic[Title/Abstract] AND floor[Title/Abstract] AND dysfunction[Title/Abstract]) OR (anxiety[Title/Abstract] AND stress[Title/Abstract] AND depression[Title/Abstract])** Filters: **Publication date from 1999/01/01 to 2014/02/07; Humans; English**	54352
#1 AND #3		311
#4	Search **((((((((((((antibacterial agents[MeSH Terms]) OR fluoroquinolones[Title/Abstract]) OR ((quinolones[MeSH Terms]) OR quinolones[Title/Abstract])) OR ((ciprofloxacin[MeSH Terms]) OR ciprofloxacin[Title/Abstract])) OR ((ofloxacin[MeSH Terms]) OR ofloxacin[Title/Abstract])) OR ((norfloxacin[MeSH Terms]) OR norfloxacin[Title/Abstract])) OR ((levofloxacin[MeSH Terms]) OR levofloxacin[Title/Abstract])) OR ((tetracyclines[MeSH Terms]) OR tetracyclines[Title/Abstract])) OR ((doxycycline[MeSH Terms]) OR doxycycline[Title/Abstract])) OR oxycyclin[Title/Abstract]) OR ((trimethoprim[MeSH Terms]) OR trimethoprim[Title/Abstract])) OR ((macrolides[MeSH Terms]) OR macrolides[Title/Abstract])) OR ((azithromycin[MeSH Terms]) OR azithromycin[Title/Abstract])) OR ((nitrofurantoin[MeSH Terms]) OR nitrofurantoin[Title/Abstract])** Filters: **Publication date from 1999/01/01 to 2014/02/07; Humans; English**	123591

#1 AND #4		172
#5	Search **(((Anti-Inflammatory Agents, Non-Steroidal[Mesh]) OR ((ibuprofen[MeSH Terms]) OR ibuprofen[Title/Abstract])) OR ((diclofenac[MeSH Terms]) OR diclofenac[Title/Abstract])) OR ((naproxen[MeSH Terms]) OR naproxen[Title/Abstract])** Filters: **Publication date from 1999/01/01 to 2014/02/07; Humans; English**	30044
#1 AND #5		28
#6	Search **((((((((((((((((((analgesics[MeSH Terms]) OR analgesics[Title/Abstract]) OR paracetamol[MeSH Terms]) OR paracetamol[Title/Abstract]) OR codeine[MeSH Terms]) OR codeine[Title/Abstract]) OR tramadol[MeSH Terms]) OR tramadol[Title/Abstract]) OR dihydrocodeine[Title/Abstract]) OR duloxetine[Title/Abstract]) OR analgesia, epidural[MeSH Terms]) OR (epidural[Title/Abstract] AND analgesia[Title/Abstract])) OR (epidural[Title/Abstract] AND anaethesia[Title/Abstract])) OR (epidural[Title/Abstract] AND anethesia[Title/Abstract])) OR amitriptyline[MeSH Terms]) OR amitriptyline[Title/Abstract]) OR nortriptyline[MeSH Terms]) OR nortriptyline[Title/Abstract]) OR gabapentin[Title/Abstract]) OR pregabalin[Title/Abstract]** Filters: **Publication date from 1999/01/01 to 2014/02/07; Humans; English**	71103
#1 AND #6		73
#7	Search **(((((((((("Adrenergic alpha-Antagonists"[Mesh]) OR (adrenergic[Title/Abstract] AND alpha-antagonists[Title/Abstract])) OR (adrenergic[Title/Abstract] AND antagonists[Title/Abstract]))) OR ((alpha[Title/Abstract] AND blockers[Title/Abstract]))) OR ((doxazosin[MeSH Terms]) OR doxazosin[Title/Abstract])) OR ((prazosin[MeSH Terms]) OR prazosin[Title/Abstract])) OR tamsulosin[Title/Abstract]) OR alfuzosin[Title/Abstract]) OR terazosin[Title/Abstract]** Filters: **Publication date from 1999/01/01 to 2014/02/07; Humans; English**	5580
#1 AND #7		88
#8	Search **(((((5-alpha Reductase Inhibitors[MeSH Terms]) OR (5-alpha[Title/Abstract] AND reductase[Title/Abstract] AND inhibitors[Title/Abstract])) OR (5-alfa[Title/Abstract] AND reductase[Title/Abstract] AND inhibitors[Title/Abstract])) OR finasteride[MeSH Terms]) OR finasteride[Title/Abstract]) OR dutasteride[Title/Abstract]** Filters: **Publication date from 1999/01/01 to 2014/02/07; Humans; English**	1665
#1 AND #8		18
#9	Search **((((((((((((((((physiotherapy[Title/Abstract]) OR ((trigger[Title/Abstract] AND point[Title/Abstract] AND release[Title/Abstract]))) OR ((myofascial[Title/Abstract] AND release[Title/Abstract]))) OR ((((global[Title/Abstract] AND relaxation[Title/Abstract])) OR (core[Title/Abstract] AND stability[Title/Abstract])) OR (breathing[Title/Abstract] AND square[Title/Abstract]))) OR ((((bladder[Title/Abstract] AND retraining[Title/Abstract])) OR (global[Title/Abstract] AND assessment[Title/Abstract] AND equality[Title/Abstract] AND movement[Title/Abstract])) OR biofeedback[Title/Abstract])) OR (((tibial[Title/Abstract] AND nerve[Title/Abstract] AND stimulation[Title/Abstract])) OR TNS[Title/Abstract])) OR ((pollen[Title/Abstract] AND extract[Title/Abstract]))) OR (((rye[Title/Abstract] AND grass[Title/Abstract])) OR cernilton[Title/Abstract])) OR ((((flavonoids[MeSH Terms]) OR flavonoids[Title/Abstract]) OR bioflavonoids[Title/Abstract]) OR quercetin[Title/Abstract])) OR (((serenoa repens[MeSH Terms]) OR (serenoa[Title/Abstract] AND repens[Title/Abstract])) OR (saw[Title/Abstract] AND palmetto[Title/Abstract]))) OR ((acupuncture therapy[MeSH Terms]) OR acupuncture[Title/Abstract])) OR complementary therapies[MeSH Terms]) OR ((exercise[Title/Abstract]) OR diet[Title/Abstract])) OR (((multi[Title/Abstract] AND disciplinary[Title/Abstract])) OR (team[Title/Abstract] OR care [Title/Abstract]))) OR ((multi-disciplinary[Title/Abstract]) AND (team[Title/Abstract] OR care [Title/Abstract]))) OR (((cognitive[Title/Abstract]) AND behavioural[Title/Abstract]) AND therapy[Title/Abstract]))) OR psychotherapy[Title/Abstract]))) OR ((hypertonic[Title/Abstract] AND pelvic[Title/Abstract] AND floor[Title/Abstract]))** Filters: **Publication date from 1999/01/01 to 2014/02/07; Humans; English**	647526
#1 AND #9		270
#10	Search **((((((((prostatectomy[MeSH Terms]) OR prostatectomy[Title/Abstract]) OR thermotherapy[Title/Abstract]) OR transurethral resection of prostate[MeSH Terms]) OR (transurethral[Title/Abstract] AND resection[Title/Abstract] AND prostate[Title/Abstract])) OR TURP[Title/Abstract]) OR transrectal high intensity focused ultrasound[MeSH Terms]) OR (high[Title/Abstract] AND intensity[Title/Abstract] AND focused[Title/Abstract] AND ultrasound[Title/Abstract])) OR (prostatic[Title/Abstract] AND massage[Title/Abstract])** Filters: **Publication date from 1999/01/01 to 2014/02/07; Humans; English**	16113
#1 AND #10		81

Supporting evidence sources

In addition to the MEDLINE database (accessed via PubMed), the following supporting sources were manually searched for relevant literature:

- The Cochrane Library
- Professional guideline groups:
  - National Institute for Health and Care Excellence (NICE)
  - Scottish Intercollegiate Guidelines Network (SIGN)
  - Royal College of Nursing (RGN)
  - British Association of Urological Nurses (BAUN)
  - British Association of Urological Surgeons (BAUS)
  - British Association of Sexual Health and HIV (BASHH)
  - NHS prostatitis map of medicine
  - British Society for Sexual Medicine (BSSM)