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Guidelines

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

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Objectives

To improve awareness and recognition of chronic bacterial prostatitis (CBP) and chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) among non-specialists and patients. To provide guidance to healthcare professionals treating patients with CBP and CP/CPPS, in both non-specialist and specialist settings. To promote efficient referral of care between non-specialists and specialists and the involvement of the multidisciplinary team (MDT).

Patients and Methods

The guideline population were men with CBP or CP/CPPS (persistent or recurrent symptoms and no other urogenital pathology for ≥3 of the previous 6 months). Consensus recommendations for the guidelines were based on a search to identify literature on the diagnosis and management of CBP and CP/CPPS (published between 1999 and February 2014). A Delphi panel process was used where high-quality, published evidence was lacking.

Results

CBP and CP/CPPS can present with a wide range of clinical manifestations. The four main symptom domains are urogenital pain, lower urinary tract symptoms (LUTS – voiding or storage symptoms), psychological issues and sexual dysfunction. Patients should be managed according to their individual symptom pattern. Options for first-line treatment include antibiotics, α-adrenergic antagonists (if voiding LUTS are present) and simple analgesics. Repeated use of antibiotics, such as quinolones, should be avoided if there is no obvious symptomatic benefit from infection control or cultures do not support an infectious cause. Early use of treatments targeting neuropathic pain and/or referral to specialist services should be considered for patients who do not respond to initial measures. An MDT approach (urologists, pain specialists, nurse specialists, specialist physiotherapists, general practitioners, cognitive behavioural therapists/psychologists, and sexual health specialists) is recommended. Patients should be fully informed about the possible underlying causes and treatment options, including an explanation of the chronic pain cycle.

Conclusion

Chronic prostatitis can present with a wide variety of signs and symptoms. Identification of individual symptom patterns and a symptom-based treatment approach are recommended. Further research is required to evaluate management options for CBP and CP/CPPS.

Keywords

guidelines, chronic bacterial prostatitis, chronic prostatitis with chronic pelvic pain syndrome, prostatitis

Introduction

Prostatitis is a common condition, with 35–50% of men reported to be affected by symptoms suggesting prostatitis during their lifetime [1,2]. Based on a population of >10 600 participants, a systematic review found an 8.2% prevalence of prostatitis symptoms [1].

The symptomatic, chronic forms of prostatitis as defined by the USA National Institutes of Health (NIH; Box 1) [3], are chronic bacterial prostatitis (CBP; NIH category II) and chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS; NIH category III). Despite having a significant negative impact on patients' quality of life (QoL) [4] and presenting diagnostic and therapeutic challenges for physicians, CBP and CP/CPPS have received relatively little attention in the literature, in comparison with other urological conditions [2]. The absence of robust and clear epidemiological data may also reflect the lack of a uniform definition and the overlap of

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Box 1 NIH classification and definition of the categories of 'prostatitis' [3].

NIH classification	Definition
I: Acute bacterial prostatitis	Acute infection of the prostate gland
II: Chronic bacterial prostatitis (CBP)	Chronic or recurrent infection of the prostate
III: Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS)	No demonstrated infection
IIIa: Inflammatory CPPS*	White blood cells in semen and/or EPS or VB3 after prostatic massage
IIIb: Non-inflammatory CPPS*	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

*EPS, expressed prostatic secretions; VB, voided bladder; VB3, post-prostatic massage voided bladder urine. *During CP/CPPS, it is possible for patients to switch between the two subcategories (IIIa and IIIb), but this has little effect on subsequent clinical management.*

symptoms with other conditions, such as benign prostatic enlargement (BPE) and prostate cancer.

Guideline and Objectives

A Prostatitis Expert Reference Group (PERG) was convened by Prostate Cancer UK, to develop consensus guidelines to improve the diagnosis and management of CBP and CP/CPPS. The main objectives of the guidelines were to:

- Provide guidance to healthcare professionals treating patients with CBP and CP/CPPS, both in non-specialist and specialist settings.
- Improve awareness and recognition of these conditions among non-specialists and patients.
- Promote efficient referral of care between non-specialists and specialists and the involvement of the multidisciplinary team (MDT).

Methods

PERG

PERG members (Appendix S1) 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 medicine, physiotherapy and psychology, as well as patient representatives. Also included were a technical team from Prostate Cancer UK and Hayward Medical Communications, with a background in communication, policy development and evidence research. The PERG met several times during the guideline development process, to discuss objectives and scope of the guidelines, assess the literature review outcomes and formulate the guidelines.

Table 1 Levels of evidence. Modified from OCEBM Levels of Evidence Working Group [5].

Level	Source of evidence
1	Meta-analysis of randomised trials
2	At least one well-designed randomised controlled study
3	Non-randomised control cohort or follow-up study
4	Case series, case-control studies, or historically controlled studies
5	Mechanism-based reasoning, expert committee reports or opinions or clinical experience of respected authorities

Literature Search

A search was conducted to identify literature on the diagnosis and management of CBP and CP/CPPS published between 1999 and 7 February 2014. 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) (Appendix S2). For the full literature search protocol see Appendix S3. References used in the guideline were graded according to the Oxford Centre for Evidence-based Medicine (OCEBM) Levels of Evidence (Table 1) [5].

Delphi Panel

Due to the limited number of published randomised controlled trials (RCTs) in CBP and CP/CPPS, the PERG concluded that the guideline would benefit from input from a supporting panel of experts. Thus, a web-based Delphi panel process was conducted to form consensus recommendations where high-quality, published evidence was found to be lacking. This anonymous and iterative group technique is designed to gather individual opinions from experts and transform these into a group consensus [6]. The Delphi panel comprised three questionnaire rounds via Survey Monkey® (for the survey questions see Appendix S4). Where consensus (agreement of ≥70% of respondents) was not achieved, input was obtained from the PERG and supporting technical team.

Results

The Delphi panel survey was circulated to 58 participants (GPs, urologists, pain specialists, nurse specialists, physiotherapists, cognitive behavioural specialists and sexual health specialists), of whom 35 (60%), 29 (50%) and 26 (45%) responded to the first, second and third rounds, respectively. All treatment recommendations that achieved consensus from the PERG or Delphi panel are shown below in bold type.

Signs and Symptoms

The wide range of clinical manifestations of CBP and CP/CPPS reflect the variety of possible underlying causes (e.g.

Table 2 Signs and symptoms reported by patients with CBP and CP/CPPS.

Pain symptoms [9–14] 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 (e.g. IBS)	Retrospective data indicate that the most prevalent localisation for pain is the perineal region (63% of patients), followed by the testicular, pubic and penile areas [14].Tests for correlations between the NIH-CPSI symptom domains suggest that urogenital pain has a greater impact on QoL than do urinary symptoms [14] IBS has been shown to be present in 22–31% of patients with CBP or CP/CPPS [13,15] and can increase the severity of pain symptoms [13,15,16]
Urinary symptoms [9,11,17–20] Voiding LUTS (weak stream, straining and hesitancy) Storage LUTS (urgency ± 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)	Cohort studies report ≥1 LUTS symptom in 39–68% of patients [17,18]. There may also be an association with recurrent UTIs in a minority of patients [19,21]
Sexual dysfunction symptoms [17,22–30] ED Ejaculatory dysfunction (premature, delayed or pain during, or after, ejaculation) Decreased libido	Findings from cohort studies (n = 130–1 800) indicate that total or partial ED is reported by 15–55% of patients with CP/CPPS [22,31–34], while the prevalence of overall, self-reported sexual dysfunction is higher at 46–92% [22,23,31,34]. Correlation studies of sexual dysfunction symptoms with NIH-CPSI scores indicate that patients with CP/CPPS with sexual dysfunction have higher total and QoL scores, suggesting that sexual symptoms can contribute substantially to morbidity [28,31–33,35,36]. However, in one study the presence of ED was shown not to independently affect symptom severity or QoL in patients with CP/CPPS [37]
Psychosocial symptoms [3,18,32,33,35,36] Anxiety or stress Depression Cognitive/behavioural consequences Decreased QoL	CBP and CP/CPPS can have a significant negative impact on QoL, potentially causing limitations to activity [38] and the QoL of patients with CBP or CP/CPPS has been shown to be as poor as that of patients with congestive heart failure or Crohn's disease [4]. Negative behavioural consequences and psychosocial symptoms, such as depression and anxiety, can also have a significant impact [39,40]. Small (n < 250) case-control studies indicate that depression, anxiety and panic disorder are significantly more common in men with chronic symptoms vs controls, using responses to the Patient Health Questionnaire (PHQ) [41] or other psychometric questionnaires (for example, the Perceived Stress Scale) [29,42,43]. Furthermore, a small (n = 61) cohort study suggests patients with CP/CPPS can experience pain catastrophising (a negative cognitive-affective response to anticipated or actual pain) and this was linked to more severe pain and QoL issues and the risk of developing chronic pain [44]

ED, erectile dysfunction; IBS, irritable bowel syndrome; UTI, urinary tract infection.

bacterial infection, inflammation and/or neurological damage) [7,8]. Table 2 [3,4,9–44] summarises the range of potential presenting symptoms, based on evidence from the literature and PERG consensus discussions. Symptoms can fluctuate considerably over time [7,8]. The four main domains are urogenital pain, LUTS (voiding or storage symptoms), psychological issues and sexual dysfunction [45].

In order to reflect the evidence base, where some treatments are recommended for use in 'early' and/or 'late' stages of CBP and CP/CPPS, consensus was sought regarding definitions of these stages.

Recommendations

- **Patients can be considered to be (i) in the early stages of the disease if they have experienced persistent, recurrent symptoms for <6 months and are antibiotic-naïve, or (ii) in the later stages of the disease if they have experienced persistent, recurrent symptoms for >6 months and are refractory to initial lines of pharmacotherapy (Level 5).**

Clinical Assessment and Diagnosis

Table 3 [11,20,38,40,46–48] summarises the investigations and physical examinations that should be considered during initial clinical assessment. Differential diagnosis is important, given the significant overlap of symptoms of CBP and CP/CPPS with those of other conditions [11,38,40]: investigations to exclude these are detailed in Table 3, with specific recommendations for Prostate Specific Antigen (PSA) testing in Box 2 [11,38,40,49].

A definitive diagnosis of CBP requires the presence of (typically recurrent) UTI and isolation of an aetiologically recognised organism from prostatic fluid or urine [38,40]. There is no 'gold standard' for a definitive diagnosis of CP/CPPS, which is typically based on patient history, symptoms and exclusion of

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

Examinations and investigations*	Setting		Rating		Comments
	Non-specialist	Specialist	Core	Optional	
Physical examinations					
DRE Including assessment of external genitalia and pelvic floor muscle dysfunction	✓	✓	✓		The bladder may be palpable if there is urinary retention; prostate may be enlarged, tender, or normal. 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 ability to fully relax between contractions. Check that symptoms are not being provoked by other structures
Abdomen To exclude other causes of abdominal pain	✓	✓	✓		
Urine dipstick and/or MSU for culture/ microscopy	✓	✓	✓		To confirm the presence of UTI and/or haematuria [11,40]
Four-glass or two-glass test†		✓		✓	To evaluate whether there is a bacterial cause, 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 EPS samples are taken for culture/ microscopy [38,46]. The two-glass test (VB2 and VB3) was shown to offer similar diagnostic sensitivity to the four-glass test [20], while other studies advocate urethral swab plus post-prostatic massage urine analysis (VB3) [47]
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 exclude differential diagnoses‡					Conditions to be excluded are: urogenital/urological/ rectal cancer; prostatic abscess; urinary tract disease (e.g. cystitis, urethritis or upper UTI); urethral stricture; BPE; obstructive calculus or foreign body; pudendal neuralgia; epididymo-orchitis; prostate tuberculosis; neurological disease affecting the bladder
PSA testing to exclude prostate cancer (refer to Box 2)	✓	✓	✓		
STI screen (e.g. via NAATs)	✓	✓	✓		
Uroflowmetry, retrograde urethrography or cystoscopy (to exclude BOO, urethral stricture or bladder neck stenosis)		✓		✓	
Prostate biopsy (only if prostate cancer suspected based on PSA level and/or DRE results)		✓		✓	
TRUS (only in refractory patients in whom prostatic abscess/other pathology suspected)		✓		✓	
Diagnostic cystoscopy (if bladder cancer suspected)		✓		✓	
Urethral swab and culture (if urethritis suspected)		✓		✓	
MRI (if prostatic abscess suspected)		✓		✓	

*BOO, bladder outlet obstruction; DRE, digital rectal examination; MRI, magnetic resonance imaging; MSU, midstream urine; NAATs, nucleic acid amplification tests; STI, sexually transmitted infection; TRUS, trans-rectal ultrasound; VB, voided bladder. *Based on information adapted from Map of Medicine. Prostatitis – Primary Care, January 2014 [11]; Map of Medicine. Prostatitis – Secondary Care, January 2014 [38]; Nickel et al. [48]; and PERG consensus. †Pursued when CBP is suspected. ‡The investigations pursued will depend on symptom presentation and patient history. N.B. Local provider services may vary for the division of assessment options across non-specialist and specialists settings.*

other causes [40]. Referral to specialist care should be considered at initial presentation if there is uncertainty regarding the possible differential diagnosis, or if severe symptoms that require immediate specialist attention are present [11].

Tools for evaluation and monitoring

Validated symptom-scoring instruments for CBP and CP/CPPS (Table 4) [50,51] include: the NIH Chronic Prostatitis Symptom Index (NIH-CPSI; evaluating pain, voiding and impact on QoL); the International Prostate Symptom Score (IPSS; urinary symptoms and impact on QoL); and the more recent Urinary, Psychosocial, Organ-specific, Infection, Neurological/systemic, and Tenderness (UPOINT) classification, that aims to stratify patients into specific symptom-led phenotypes [50]. The five-item version of the International Index of Erectile Function (IIEF-5) or Sexual Health Inventory for Men (SHIM) specifically evaluate ED.

Box 2 PSA testing recommendations. Adapted from information with the Prostate Cancer Risk Management Programme [49]. The Prostate Cancer UK booklet [112] provides relevant patient information for PSA testing.

PSA testing should be considered to exclude prostate cancer under the following circumstances:

- Abnormal prostate on DRE
- Symptoms suggest BOO secondary to BPE [11,38,40]
- Patient concern in relation to prostate cancer

Timing:

PSA testing should be postponed for:

- 6 weeks after treatment for UTI
- 1 week after DRE
- 48 hours after vigorous exercise or sexual activity
- 6 weeks after prostate biopsy
- 2 weeks after flu-like symptoms

Age-specific threshold PSA level measurements for prostate cancer risk management:

- 50–59 years: ≥3.0 ng/mL
- 60–69 years; ≥4.0 ng/mL
- ≥70 years: ≥5.0 ng/mL
- No age-specific ranges for men aged ≥80 years
- Refer to local laboratory upper limits of normal

Treatment effects

- If assessing PSA levels in a patient receiving a 5α-reductase inhibitor, note that a rapid decrease in PSA levels occurs within the first few months of treatment. After 6 months of treatment, PSA will have decreased by ≈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 level results with care
Caution is required with results interpretation, since PSA levels are prostate- rather than prostate cancer-specific and levels can be elevated in/by:

- Prostate enlargement
- Prostate cancer
- Infection or inflammation
- Physical causes – vigorous exercise (e.g. cycling), DRE, prostate biopsy
- A normal prostate

Recommendations

- **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).**

Psychosocial screening

CBP and CP/CPPS can negatively impact QoL [4] and lead to negative behavioural consequences [18,29,39,40,42]. Moreover, men reporting a previous history of sexual, physical or emotional abuse were more likely to have symptoms suggesting CP/CPPS, and previous abuse increased both the NIH-CPSI pain and urinary scores [52]. The Delphi approach was used to reach a consensus on the implementation of psychosocial screening.

Table 4 Validated questionnaires for assessment of CBP and CP/CPPS.

NIH-CPSI (http://backinmotionpt.com/wp-content/uploads/2010/03/mens_pfcpsi-.pdf)	Nine-item questionnaire (total score 0–43) measuring: • Pain (four questions evaluating pain location, frequency and severity, 0–21) • Voiding (two questions evaluating voiding and storage symptoms, 0–10) • Impact on QoL (three questions, 0–12)
IPSS (http://www.urospec.com/uro/Forms/ipss.pdf)	Eight-item questionnaire measuring: • Urinary symptoms (seven questions evaluating incomplete bladder emptying, frequency, intermittency, urgency, weak stream, straining and nocturia, 0–35) • Impact on QoL (one question, 0–6)
UPOINT [50]	Aims to stratify patients into specific symptom-led phenotypes. Measures urinary symptoms, psychosocial dysfunction, organ-specific findings, infection, neurological/systemic routes, and tenderness of muscles [50] Has been used to inform phenotypically directed multimodal treatment in CP/CPPS [51]
IIEF-5 or SHIM (http://surgery.arizona.edu/sites/surgery.arizona.edu/files/pdf/SHIM%20score.pdf)	Five-item questionnaire for screening and diagnosis of ED (past 6 months of symptoms)

Recommendations

- **Patients should be screened for psychosocial symptoms (e.g. anxiety or stress) using either the psychosocial yellow flag system and/or Patient Health Questionnaire-9 (PHQ-9) and/or Generalised Anxiety Disorder-7 (GAD-7) scales (Box 3). If a clinically relevant level of psychosocial symptoms is observed, referral to a psychosocial specialist (e.g. psychiatrist, specialist psychologist or cognitive behavioural therapist) should be considered (Level 5).**

Patient communications

It is important that the diagnosis, aetiology and management approaches are discussed with the patient; consensus gained via the Delphi approach recommends the following:

Recommendations (all Level 5)

- **At first presentation, other concerns or differential diagnoses, including urological cancers and infertility,**

Box 3 Psychosocial assessment.

Validated questionnaires

- *Patient Health Questionnaire-2 (PHQ-2, http://www.commonwealthfund.org/usr_doc/PHQ2.pdf)* – a two-item questionnaire to assess the frequency of depressed mood over the past 2 weeks
- *Patient Health Questionnaire-9 (PHQ-9, http://phqscreeners.com/pdfs/02_PHQ-9/English.pdf)* – a nine-item questionnaire to assess the frequency of depressed mood over the past 2 weeks
- *Generalised Anxiety Disorder-7 (GAD-7, http://phqscreeners.com/pdfs/03_GAD-7/English.pdf)* – a seven-item questionnaire to assess the severity of generalised anxiety disorder over the past 2 weeks.
- *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?

Questions for treatment-refractory patients

Life event screening questions:

- Have you recently undergone any major life events; e.g. 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?

should be discussed with the patient to establish a full patient history and help inform future investigations.

- **When diagnostic tests for a bacterial cause have been confirmed, the results need to be clearly communicated to the patient, who must be informed of both positive and negative results of diagnostic tests and implications for future treatment.**
- **Patients should be informed of the underlying causes of CBP and CP/CPPS to help improve their understanding. This may include an explanation of basic pelvic anatomy, the chronic pain cycle, and potential routes for pain (neuropathic vs nociceptive).**

Reliable sources for patient information include those available through the Prostate Cancer UK website (Appendix S2).

Treatment Strategies

Table 5 [9,22,48,53–108] summarises the results of the literature search on interventions for CBP or CP/CPPS.

α-adrenergic antagonists ('α blockers')

Most of the placebo-controlled RCTs that evaluated α-adrenergic antagonists (tamsulosin, alfuzosin, doxazosin, terazosin and silodosin) in CBP or CP/CPPS found significant reductions in symptoms and/or improvement in QoL scores (Table 5). These findings have contributed to widespread use of these agents in these settings, although their clinical significance has been questioned [64].

Recommendations

- **α-adrenergic antagonists 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).**

There is a lack of evidence to inform best practice for the use of these agents and the Delphi panel process was used to reach a consensus.

Recommendations (Level 5)

- **Treatment with α-adrenergic antagonists should be considered in patients who present with significant voiding LUTS (e.g. slow urinary flow, hesitancy).**
- **If no relief from voiding LUTS or other symptoms of CBP or CP/CPPS is achieved within 4–6 weeks, treatment should be stopped and a different pharmacotherapy considered. Patients should be referred to specialist care if other approaches have been exhausted.**
- **Due to the adverse side-effect profiles of this class of drugs, consider offering uroselective α-adrenergic antagonists (e.g. tamsulosin, alfuzosin and silodosin) as first-line treatment in patients with CBP and CP/CPPS who present with voiding LUTS (Level 5).**

Antibiotics

A wide spectrum of microbial strains may cause infection in CBP (Box 4) [9]. Despite the widespread use of antibiotics in patients with CBP and CP/CPPS, evidence to support their use in these populations is relatively weak. Ciprofloxacin, levofloxacin, azithromycin, doxycycline, and clarithromycin are reported to be effective in eradicating infection and/or improving symptoms in CBP, although there is a lack of prospective, head-to-head placebo-controlled trials to guide choice of agent (Table 5). Table 6 [9,109] summarises key features of the different antibiotic classes. The quinolones (e.g. ciprofloxacin and levofloxacin) are considered the antibiotics of choice because of their favourable pharmacokinetic properties [9].

Many patients without confirmed infection respond to antibiotic intervention, possibly reflecting an anti-inflammatory or anti-neuropathic effect of the antimicrobial agent. Available evidence indicates that antibiotics can provide symptom improvement in patients with CP/CPPS (Table 5).

Table 5 Interventions for CBP and CP/CPPS: results of literature search.

α-adrenergic antagonists	In all, 10 placebo-controlled RCTs (n = 58–272) were identified that evaluated α-adrenergic antagonists (tamsulosin [53–55], alfuzosin [56,57], doxazosin [58,59], terazosin [60,61] and silodosin [62]) in CBP and CP/CPPS. Most (eight) showed positive results, with significant differences vs placebo in NIH-CPSI total, urinary symptom, pain, and/or QoL scores [54–57,59,60], or in scores using other validated symptom scoring tools [58,61]. However, there was heterogeneity in primary endpoints, patient eligibility criteria (e.g. previous exposure to α-blockers) and trial duration (1.5–6 months). A recent systematic review and network meta-analysis of α-blocker RCTs found significant differences vs placebo in total, pain, voiding and QoL NIH-CPSI scores [63]. However, another recent systematic review questioned the clinical significance of these reductions [64]. Notably, two of the larger, placebo-controlled trials that evaluated tamsulosin (n = 196) [53] and alfuzosin (n = 272) [57] failed to show any significant difference in total NIH-CPSI scores, the only outcome achieving statistical significance being the score for ejaculation on the Male Sexual Health Questionnaire (P = 0.04) in the alfuzosin trial. Possible reasons include the short treatment duration (≤12 weeks) and/or inclusion of refractory patients with previous exposure to α-blockers [57]
Antibiotics	**CBP** Despite the widespread use of antibiotics in patients with CBP and CP/CPPS, evidence in a CBP population primarily exists within RCTs or retrospective comparative trials lacking placebo control. Microbiological eradication rates were 40–77% for ciprofloxacin [65–67], 75% for levofloxacin [65], 80% for azithromycin [66,68,69], 77% for doxycycline [68], 80% for clarithromycin [69], and 62–77% for azithromycin + ciprofloxacin (depending on ciprofloxacin dose) [70]. Higher eradication rates (>90%) were reported with azithromycin and levofloxacin either alone, in combination or sequentially, depending on the locality of infection (urethral, prostatic or both) in patients with CBP with *C. trachomatis* infection [71]. Significant differences in symptom severity, as assessed by changes in NIH-CPSI scores, were seen between baseline and the end of treatment in two trials [70,71]. Others reported improvements in clinical outcomes but failed to use validated tools to report these [65–69] Of the identified comparative studies in patients with CBP, one (n = 408) found that levofloxacin offered advantages over ciprofloxacin for bacterial eradication rates and clinical improvement [67], while another of similar size (n = 377) and design showed no significant differences between these agents [65]. Azithromycin was reported to be more effective than ciprofloxacin in the treatment of *C. trachomatis* infections [66]. 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 (Table 6). The quinolones, such as ciprofloxacin and levofloxacin, are considered the antibiotics of choice because of their favourable pharmacokinetic properties [9]. Another antibiotic agent, fosfomycin, achieves reasonable intraprostatic tissue levels and is active against extended-spectrum β-lactamase producing organisms; it can be considered in patients with multiresistant Gram-negative infections, based on susceptibility results and discussion with local microbiologists **CP/CPPS** Only three small-to-medium sized (n = 48–196), adequately designed RCTs, which assessed ciprofloxacin [53], levofloxacin [48], and tetracycline hydrochloride [72] vs placebo in patients with CP/CPPS, were identified. Although symptom improvement was observed, the ciprofloxacin study failed to show a statistical difference in NIH-CPSI total score from baseline to 6 weeks in a CP/CPPS population [53]. Similar results were observed in the levofloxacin study; while symptom improvement with antibiotic treatment was seen, the results failed to achieve significance vs placebo, either at end of treatment (6 weeks) or follow-up (12 weeks) vs baseline [48]. However, the average time from diagnosis of CP/CPPS was 6.2 years [53] and 6.5 years [48], respectively, at study entry. Such patients may represent a treatment-refractory phenotype for which antibiotic therapy may not be appropriate. Low patient numbers may also have contributed to the lack of significance. More promising results were observed in a comparison of tetracycline hydrochloride vs placebo, with significant differences in NIH-CPSI scores and bacterial eradication rates; however, patient numbers were small (n = 48) [72]. Recent direct meta-analyses of these trials showed that antibiotics provide symptom improvement, but not at a significant level [63, 64] Evidence from small (n = 20–105), randomised, comparative trials provides mixed support for using antibiotics in CP/CPPS, with significant differences from baseline in symptoms observed using levofloxacin [73], but not ciprofloxacin [74]; however, the ciprofloxacin study imposed a stringent significance threshold (P < 0.001)
Pain pharmacotherapies	Published evidence on the use of pharmacotherapy for treatment of pain in CBP and CP/CPPS populations is scarce. Only two RCTs were identified for NSAIDs, one of which evaluated rofecoxib [75] (now withdrawn from the market). The second RCT evaluated celecoxib in patients with CP/CPPS, with a statistically significant decrease in NIH-CPSI total (P < 0.015), pain (P < 0.006) and QoL (P < 0.032) scores after 2, 4 and 6 weeks; however, the effects were limited to the short duration of therapy [76]. An RCT (n = 50) evaluated ibuprofen vs a terpenic mixture (Rowatinex®) in CP/CPPS; ibuprofen (n = 25) was associated with a significant improvement from baseline in total, pain and QoL NIH-CPSI scores after 6 weeks' treatment, but was outperformed by the terpene mixture [77]. However, the small study size and lack of a placebo arm are caveats. 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% CI 1.2–2.6), based on the combination of three trials evaluating rofecoxib, celecoxib and a corticosteroid [63]. The second analysis, based on only the rofecoxib and celecoxib trials, concluded that no significant differences in efficacy could be ascertained for NSAIDs vs placebo [64] 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) vs placebo (n = 106) in the CP/CPPS population [78]. Compared with the placebo group, patients in the pregabalin arm had reductions in the NIH-CPSI total score and subscores (P < 0.05). However, pregabalin therapy for 6 weeks was not superior to placebo in the rate of a 6-point decrease in the NIH-CPSI total score [78]

Table 5 (continued)

5α-reductase inhibitors	The evidence-base for the use of 5α-reductase inhibitors in CP/CPPS is limited, with only three small (n = 41–76) RCTs identified, which evaluated finasteride [79–81]. The first study reported showed that finasteride significantly reduced pain and voiding symptoms vs baseline; however, no statistically significant differences vs a small and non-comparable control group were seen, which was probably due to lack of power [80]. A later study, which compared finasteride with *Serenoa repens* (saw palmetto), showed that patients treated with finasteride had a significant and durable improvement (1-year trial duration) in NIH-CPSI total and pain domains, but not for urinary symptoms, when compared with baseline [79]. However, the trial size (n = 64) and lack of a placebo arm are notable caveats. A third study showed better outcomes, via measurements of subjective overall assessment and NIH-CPSI scores, for finasteride vs placebo, but the results were not statistically significant [81] 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 aged >60 years with PSA levels >3.0 ng/mL), the REduction by DUtasteride of prostate Cancer Events (REDUCE) study prospectively examined the effect of dutasteride vs 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 6 months for 4 years) [82]. NIH-CPSI total score decreased significantly at 48 months in the dutasteride group vs placebo in men with prostatitis-like pain (n = 678, P < 0.001) 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 vs placebo for both prostatitis subgroup populations assessed [82]. 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 that use of 5α-reductase inhibitors in older (aged ≥50 years) patients with PSA levels of >2.5 ng/mL (for those aged 50–60 years) or >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 As described in the full NICE clinical guidelines for the management of LUTS in men [83], a larger body of RCT evidence has evaluated the use of 5α-reductase inhibitors to treat LUTS in men with BPE; such guidelines are listed in Appendix S2
Combined/multimodal therapy	The treatment combination most frequently evaluated has been that of α-blocker and antibiotic therapy. In a placebo-controlled trial, which compared tamsulosin vs ciprofloxacin vs a combination of both over 6 weeks in CP/CPPS, the total NIH-CPSI scores demonstrated significant mean improvement of 3–6 points from baseline in all treatment groups. However, no statistically significant differences between treatment groups were seen [53]. Similar results were obtained in a comparison of doxazosin, levofloxacin and a combination of both, with the multimodal arm failing to provide any additional benefit over monotherapy [84]. However, small (n ≤ 105) comparative trials evaluating combinations of tamsulosin plus levofloxacin [73] and doxazosin plus ciprofloxacin [74] have shown that combined therapies outperformed monotherapy approaches in terms of NIH-CPSI score improvements. Evaluations of three- or four-component combinations of antibiotic, α-blocker, phytotherapy and/or physiotherapy techniques provide data in favour for combined therapies [51,85,86]; however, the lack of a control arm in these studies is a notable caveat
Specialist physiotherapy	Three small (n = 19–31) pilot studies [87–89] have shown that 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, showed a mean reduction in the total NIH-CPSI score from 23.6 at baseline to 11.4 after treatment (P < 0.001) [88]. Other small-to-medium studies suggest symptom improvement can be achieved by combining myofascial trigger point release with paradoxical relaxation training [22,90,91]. A small (n = 24) randomised, placebo-controlled trial in patients with CP/CPPS found that TENS was significantly more effective than placebo in reducing in pain symptoms [92] Small pilot studies of acupuncture in patients with CP/CPPS refractory to standard pharmacotherapy have provided positive results; in 12 men, a 6-week acupuncture regimen (given twice weekly), achieved a significant decrease in total, pain, urinary and QoL NIH-CPSI scores after an average 33 weeks follow-up (P < 0.05) [93]. Similarly, symptom improvements, as assessed by the NIH-CPSI, were seen with a 5-week [94] and 6-week course [95] of acupuncture (on the bilateral BL33 region), with improvements in pain, voiding symptoms and QoL in non-inflammatory CP/CPPS. Randomised, sham-controlled studies (n = 39–89) support these results; a 10-week course of acupuncture proved almost twice as likely as sham treatment to improve CP/CPPS symptoms [96], while a three-arm trial showed that after 6 weeks of electro-acupuncture, the NIH-CPSI total score had decreased significantly vs the sham and advice and exercise groups alone (P < 0.001) [97]. A recent review of the evidence on the use of acupuncture in prostatitis concluded that the findings should encourage healthcare providers to use acupuncture to manage pain in CP/CPPS, in conjunction with standard treatment [98]
Phytotherapy	Three small RCTs were identified that evaluated phytotherapy in CP/CPPS [99–101]. In a trial of a rye pollen extract (Cernilton) (n = 70) vs placebo (n = 69), the pollen extract significantly improved total, pain and QoL NIH-CPSI scores in patients with inflammatory CP/CPPS vs placebo, without any severe adverse effects [101]. Significant differences between another pollen extract (Prostat/Poltit) and placebo were demonstrated in a small (n = 60) trial, but a validated tool for symptom scoring was not used [99]. 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 vs placebo, with the improvement in total score resulting from improvements in the pain score (from 10.3 to 6.2, P = 0.005) and QoL score (from 8 to 4.9, P = 0.004) but not the urinary score (from 2.7 to 1.5, P = not significant) [100]. A recent network meta-analysis of these trials indicated that phytotherapy offers a favourable response rate vs placebo (RR 1.6, 95% CI 1.1–2.4) [63] 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) [102]. However, patients with CP/CPPS treated with *Serenoa repens* reported no appreciable long-term improvement in NIH-CPSI scores in a 1-year comparative study vs finasteride [79]. The only trial in the CBP population compared the addition of four phytotherapy agents (*Serenoa repens*, *U. dioica*, curcumin and quercetin) to antibiotic treatment vs antibiotic treatment alone; significant differences in favour of the combined treatment were seen [103]

Table 5 (continued)

Surgical intervention	Results of small ($n < 40$) pilot studies suggested that TUNA [104] and transurethral microwave thermotherapy [105] offered some symptom improvement compared with baseline in patients with CP/CPPS, 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 [106]. The largest study in this review evaluated two subgroups receiving either a combination of antibiotics and tri-weekly prostatic massage for 1 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 seen after treatment. However, no difference was recorded between the scores after treatment of patients who did or did not receive repeated prostatic massage [107]. The review concluded that the available studies do not provide high-quality evidence, due to the lack of randomised placebo/sham-controlled trials [106]. In addition, no two studies have used the same protocol or tool for outcome measurement, thus preventing the pooling of data [106]. Neuromodulation via sacral nerve stimulation has also been reported to reduce pelvic pain with one sham-controlled medium-sized study ($n = 89$) providing support; 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 [108]

RR, relative risk, NSAIDs, non-steroidal anti-inflammatory drugs.

Box 4 Pathogens implicated in prostatitis. Adapted from Grabe et al. [9].

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

May cause CBP in those with immunodeficiency

Mycobacterium tuberculosis
Candida species
Rare pathogens e.g. Coccidioides immitis, Blastomyces dermatitidis, Histoplasma capsulatum

Recommendations

- **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, taking into consideration 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 (all Level 5):

- **For patients with early-stage CBP and CP/CPPS, offer a quinolone (e.g. ciprofloxacin or ofloxacin) for 4–6 weeks as first-line therapy.**
- **A repeated course of antibiotic therapy (4–6 weeks) should be offered only if a bacterial cause is confirmed or if there is a partial response to the first course.**
- **If a bacterial cause is excluded (e.g. via urine dipstick or culture) and symptoms do not improve after antibiotic therapy, a different treatment method or referral to specialist care should be considered.**

Pain management

Published evidence on the use of pharmacotherapy for treatment of pain in CBP and CP/CPPS is scarce (Table 5). Given the link between CP/CPPS and neuropathic pain [39,78,110], guidance should be sought from the NICE clinical guideline on the pharmacological management of neuropathic pain [111] if neuropathic pain is suspected. The involvement of, or referral to, a specialist pain team should be sought in such cases. Table 7 [109] summarises pharmacotherapy options that may be considered for the treatment of neuropathic pain.

Due to a lack of published RCT evidence for the use of pain medications in CBP and CP/CPPS, the Delphi panel approach was used to reach a consensus on best practice for the treatment of pain symptoms in the early stages of these conditions.

Recommendations (All Level 5)

- **In patients with early-stage disease who present with pain symptoms, regular paracetamol may be offered.**
- **NSAIDs should be offered only for short-term treatment of pain, to patients with early-stage CBP or CP/CPPS whose symptoms are suspected to be due to an inflammatory process, or those judged to be experiencing an inflammatory flare. These patients should be under regular review by a GP.**
- **To prevent unwanted adverse effects, NSAIDs should be stopped within 4–6 weeks of treatment initiation if they do not reduce symptoms.**

Table 6 Antibiotic treatment options. Based on information adapted from Grabe et al. [9], the British National Formulary [109] and PERG expert consensus.

Antibiotic	Advantages	Considerations	PERG recommendation
Quinolones: e.g. Ciprofloxacin	Favourable pharmacokinetic profile, with good bioavailability and excellent penetration into prostate. Good activity against typical and atypical pathogens	Drug interactions; Phototoxicity; CNS adverse events (depending on choice of agent), tendonitis	Consider – first-line (Level 5) Dose and duration should be sufficient to eradicate the infection, e.g. ciprofloxacin 500 mg BID × 28 days
Trimethoprim	Active against most relevant pathogens. Monitoring unnecessary. Good penetration into 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. 200 mg BID × 28 days
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 BID × 28 days
Macrolides: e.g. Azithromycin	Good penetration into prostate Active against *Chlamydia* and Gram-positive bacteria	Minimal supporting data from RCTs. Unreliable activity against Gram-negative bacteria	Reserve for special indications, based on advice from microbiologist and microbiological findings

BID, twice daily (bis in die).

Table 7 Treatment options for neuropathic pain. Based on information from the British National Formulary [109] and PERG expert consensus.

Analgesic class	Drug name	Starting dose	Maintenance dose	Common adverse effects	PERG practical points
Gabapentinoids	Gabapentin	100–300 mg at night	600 mg TID	Dizziness, sedation, dyspepsia, dry mouth, ataxia, peripheral oedema, weight gain	(Level 5) Few drug interactions. Safe in overdose. Gut transport mechanism can become saturated, limiting absorption from gastrointestinal tract
	Pregabalin	50–75 mg at night	300 mg BID	Dizziness, sedation, dyspepsia, dry mouth, ataxia, peripheral oedema, weight gain	(Level 5) 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	(Level 5) Many patients obtain pain relief at lower dose
	Duloxetine	30 mg in evening (or in morning, if insomnia)	60–120 mg QD	Nausea, sedation, insomnia, headache, dizziness, dry mouth, constipation	(Level 5) Less sedating. May cause insomnia in some patients

BID, twice daily (bis in die); QD, once-daily (quaque die); SNRI, serotonin-noradrenaline (known in the USA as norepinephrine) reuptake inhibitor; TID, three times daily (ter in die).

- **In patients with early-stage CBP or CP/CPPS, use of opioids for pain management should be avoided, due to the risk of dependency.**
- **If pain is considered to be neuropathic in origin, treatment with a gabapentinoid (e.g. pregabalin or gabapentin), a tricyclic antidepressant (e.g. amitriptyline, nortriptyline or trimipramine) or a selective serotonin-noradrenaline (known in the USA as norepinephrine) reuptake inhibitor (SNRI; e.g. duloxetine) is warranted (Table 7).**

5α-reductase inhibitors

Evidence for the use of 5α-reductase inhibitors in CP/CPPS is very limited. Some improvements in symptomology were noted in small studies with finasteride (Table 5) and also a larger study with dutasteride in older patients with prostatitis-like pain or syndrome who were judged to be at risk of prostate cancer [PSA level of >2.5 ng/mL (aged 50–60 years) or >3.0 ng/mL (aged >60 years)] [82]. As noted in the full NICE clinical guidelines for the management of LUTS in men [83], there is a larger body of RCT evidence for use of 5α-reductase inhibitors to treat LUTS in men with BPE (Appendix S2).

Recommendation

- **There is insufficient evidence to warrant recommending 5α-reductase inhibitors as monotherapy in CP/CPPS, unless co-existing BPE is present (Level 2).**

Combined/multimodal therapy

Using multiple interventions to target different symptom areas simultaneously may be expected to provide a more beneficial approach than monotherapy. The treatment combination most frequently evaluated has been that of α-blocker and antibiotic therapy. Data are limited, with conflicting findings (Table 5). The Delphi panel approach was, therefore used to reach a consensus.

Recommendation (Delphi panel)

- **Multimodal/combined therapy should be uniquely designed for each individual patient, according to history, physical examination and investigations. Depending on the symptoms at presentation, the following may be considered for adding to first-line antibiotic therapy (all Level 5).**
  - An α-blocker and/or an NSAID.
  - An agent targeting neuropathic pain (e.g. pregabalin).
  - A 5α-reductase inhibitor (predominantly for patients with coexisting LUTS with BPE).

Follow-up and Treatment of Refractory Symptoms

Patients should be followed-up 4–6 weeks after their first presentation. 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. The management strategy should be guided by symptoms.

Recommendations (All Level 5)

- **If a bacterial cause is excluded and no symptom improvement is observed after antibiotic therapy, a different treatment method or referral to specialist care should be considered.**
- **Patients who are refractory to treatment should be questioned about the possibility of any past trauma (including physical, emotional or sexual abuse; questions about abuse should only be implemented if the treating clinician has sufficient skills and resources to manage patients who have experienced abuse).**
- **An MDT approach is recommended, with pharmacotherapy, physical and psychosocial approaches being integrated into a holistic treatment programme individualised for the patient.**
- **The MDT may include urologists, pain specialists, nurse specialists, physiotherapist, GPs, cognitive behavioural/psychological therapists and sexual health specialists.**

Pain management

With any pain condition, delayed recovery can lead to chronicity, compromised physical function and development of psychosocial sequelae. If neuropathic pain is suspected, this should be addressed with consideration of pharmacological strategies as already outlined above (Table 7).

Recommendations (PERG)

- **When pain is severe and refractory to the treatments outlined in Table 7, or is significantly impairing the patient's lifestyle and ability to participate in daily activities, referral to a specialist pain service should be considered (Level 5).**

The role of the pain service is to provide a multidisciplinary assessment of the patient and formulate an individualised therapeutic management plan combining treatment of pain, physical disability and psychosocial co-morbidity (Box 5).

Specialist physiotherapy

The symptoms of CBP and CP/CPPS may result from physical dysfunction, such as abnormal pelvic muscle spasm and muscle tenderness [10,12]. Therapies that aim to improve relaxation and coordinated use of the pelvic floor muscles, such as biofeedback physical therapy and pelvic floor re-education, as well as myofascial trigger point release, may play a role in providing symptom improvement in patients with CP/CPPS (Table 5). Several studies of acupuncture have provided positive results (Table 5). Transcutaneous electrical nerve stimulation (TENS) [92] was also reported to be beneficial. As most of this evidence is derived from small proof-of-principle or pilot studies, and little is reported on best practice approaches, the Delphi process was used to reach a consensus.

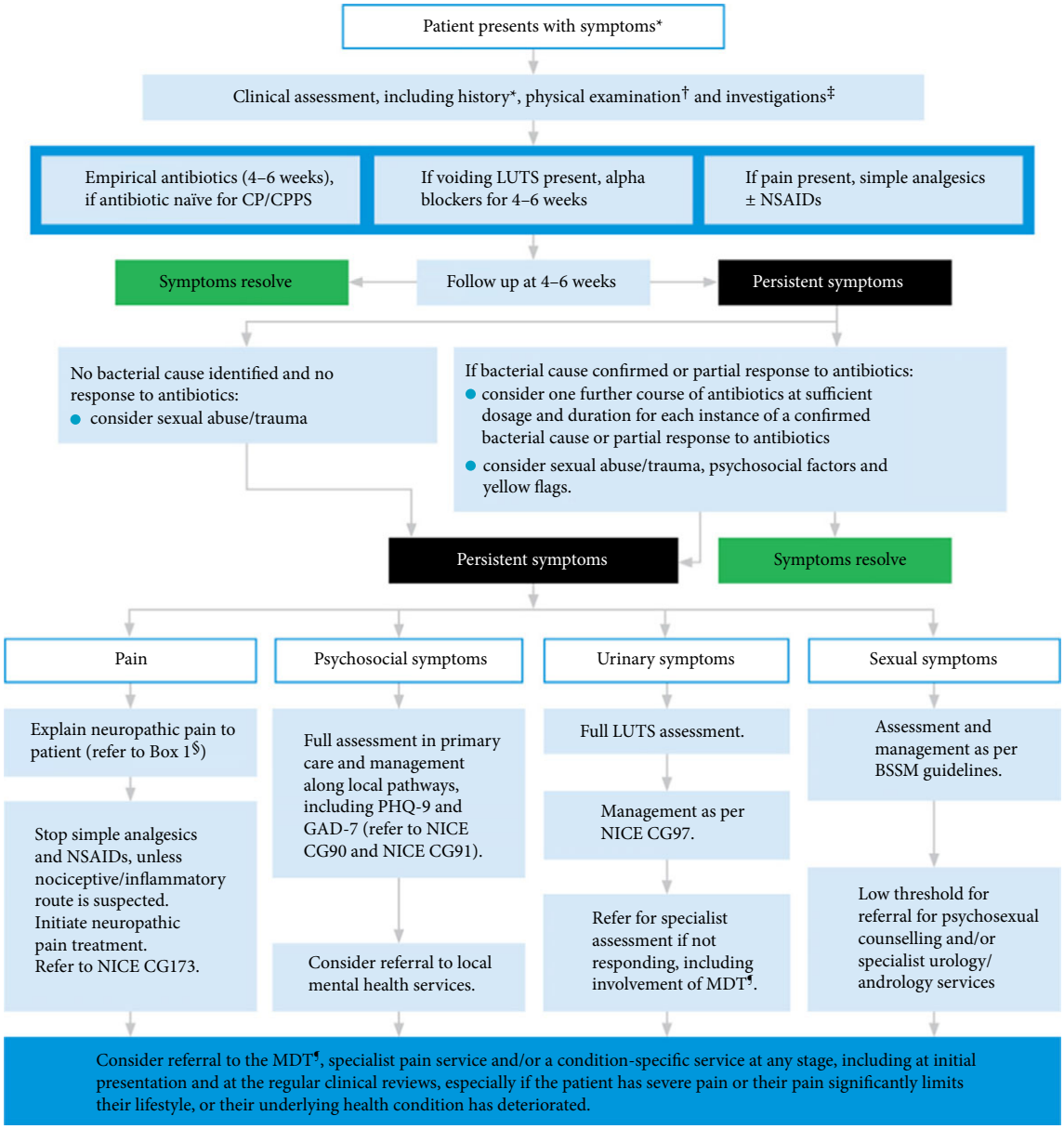
Recommendations (All Level 5)

- **Before referral to specialist physiotherapy, a number of diagnostic tests (e.g. sexually transmitted infection**

Box 5 Pain management services.

- Surgical pain interventions; e.g. 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 anti-neuropathic medications
- Intensive and individualised specialist physical therapy or psychology
- Neuromodulation procedures (e.g. 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

Fig. 1 Treatment algorithm for the diagnosis and management of CBP and CP/CPPS. In patients describing typical neuropathic pain symptoms (e.g. 'burning', 'shooting' pain), or in any patient with persistent pain (>3 months), consider the possibility of neuropathic pain and treatment with appropriate anti-neuropathic medication strategies.



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 examinations, musculoskeletal assessment.
‡ Investigations (**see Table 1**): 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.
§ Box 1can be found in the full version of the guideline:
http://prostatecanceruk.org/media/2403685/prostate-cancer-uk-chronic-prostatitis-guideline-full-sep-2014.pdf
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: http://www.nice.org.uk/guidanca/cg91/resourcest/guidancedepression-in-adults-with-a-chronic-physical-health-problem-pdf
NICE CG97: http://www.nice.org.uk/guidanca/cg91/resourcest/guidancedepression-in-adults-with-a-chronic-physical-health-problem-pdf
BSSM guidelines: www bssm.org.uk/downloads/BSSM ED Management Guidelines 2013.pdfa

screen, culture/microscopy of voided bladder urine, urethral smear, nucleic acid amplification test and relevant pelvic physical examinations; Table 3) should be conducted to confirm a physical causative route, and exclude non-physical causes, for symptoms.

- **After referral, a full assessment (e.g. symptom score scaling, examination of the pelvic floor muscles) should be completed to guide the subsequent sequence of physiotherapy treatments.**
- **If the patient presents with psychosocial symptoms, a planned therapeutic strategy involving stress management (including explanation of the chronic pain cycle) should be considered, in addition to seeking advice from the patient's GP or urologist regarding potential onward referral to a psychosocial specialist.**
- **The following specialist physiotherapy treatment options may be considered: pelvic floor re-education; local pelvic floor relaxation; biofeedback; general relaxation; deep relaxation/mindfulness; trigger point release; myofascial release; stretches; exercise for pain management; TENS; acupuncture for trigger point release and pain management; bladder retraining.**

The Delphi panel did not reach a consensus on a number of specialist physiotherapy techniques (core stability training, diaphragmatic breathing exercises, acupuncture for urgency, abdominal massage for constipation, and defaecation techniques), although it was felt that they might be suitable for certain patients, according to symptoms.

Phytotherapy

Various phytotherapies, including pollen extracts, bioflavonoids and/or *Serenoa repens* (saw palmetto) have been reported to improve clinical symptoms in small studies in patients with CBP or CP/CPPS (Table 5).

Recommendations

- **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 (CBT) and psychotherapy

While it is recognised that psychosocial symptoms may be part of CBP and CP/CPPS [29,41–43], no evidence from RCTs or comparative studies is available to support the use of psychological treatment or CBT in these settings. The Delphi process was used to reach a consensus regarding best practice for these techniques.

Recommendations (Level 5)

- **Psychosocial symptoms should be assessed in both 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.**
- **CBT should be considered in conjunction with other treatments in later-stage CBP and CP/CPPS, as it may improve pain and QoL.**

Surgical interventions

The evidence on surgical management techniques such as prostatectomy, transurethral resection of the prostate (TURP), transrectal high-intensity focused ultrasound (HIFU), transurethral needle ablation (TUNA) of the prostate, and transurethral microwave thermotherapy in CP/CPPS is very limited (Table 5). Repetitive prostatic massage has also been evaluated and the potential usefulness of this technique (with or without a general anaesthetic) in refractory patients was put to the Delphi panel but no consensus was reached. Neuromodulation techniques, such as sacral nerve stimulation [108], have been reported as being successful in treating CP/CPPS but, again, most of this evidence is derived from small proof-of-principle or pilot studies and, to date, little is reported on best practice approaches.

Recommendations

- **There is insufficient evidence to warrant recommending surgical techniques, including radical prostatectomy, TURP, HIFU or prostatic massage for the treatment of CBP or CP/CPPS, except in the context of a clinical trial setting (Level 3).**

Figure 1 provides an algorithm for the diagnosis and management of CBP and CP/CPPS. This summarises the

Table 8 Priorities for management of CBP and CP/CPPS.

Patients should be managed according to their individual symptom pattern – no single management pathway is suitable for all patients
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 cause
Early use of medication targeting neuropathic pain should be considered for all patients who are refractory to initial treatments. If neuropathic pain is suspected, ensure a prompt referral to an MDT that includes pain specialists
Early referral to specialist services should be considered when patients fail to respond to initial measures
An MDT approach should be implemented, including urologists, pain specialists, nurse specialists, specialist physiotherapists, GPs, cognitive behavioural therapists/psychologists and sexual health specialists
Patients should be fully informed about possible underlying causes and treatment options

consensus recommendations of the PERG and Delphi panel, as presented above.

Discussion

We have developed consensus guidelines aimed at improving the diagnosis and management of CBP and CP/CPPS. Full and 'quick reference' versions of the original guidelines are available from the Prostate Cancer UK website (http://prostatecanceruk.org/prostatitisguideline). The quick reference version is also available at http://www.bjuinternational.com/?p=21102. These guidelines were issued in 2014 and will be considered for review in 3 years' time, unless relevant evidence updates suggest otherwise.

Priorities for implementation are listed in Table 8. We conclude that further research is required to evaluate the following:

- Multimodal pharmacotherapy for patients with CP/CPPS who are refractory to initial mono-pharmacotherapy approaches.
- 5α-reductase inhibitors in CP/CPPS, especially in older patients (aged >50 years) and/or those at increased risk of prostate cancer (aged 50–60 years with PSA levels of >2.5 ng/mL or aged >60 years with PSA level of >3.0 ng/mL).
- The cost impact and effectiveness of interventions to treat CBP and CPPS.
- The effectiveness of a multidisciplinary approach and symptom-based management vs 'usual care' for patients with CBP and CP/CPPS.
- Phosphodiesterase type 5 (PDE5) inhibitors for those with sexual dysfunction.
- The prevalence and impact of psychosocial issues and other co-morbidities e.g. irritable bowel syndrome (IBS).

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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 and was not used for the development of this guideline. Hayward Medical Communications received funding from Prostate Cancer UK to manage the literature review, web-based Delphi process and development of the original guideline. Julia Balfour received Prostate Cancer UK funding for editorial support. All PERG members and Delphi panel members participated in the process on a voluntarily basis. Jon Rees (PERG chair) has conducted 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.

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Abbreviations: BOO, bladder outlet obstruction; BPE, benign prostatic enlargement; BSSM, British Society for Sexual Medicine; CBP, chronic bacterial prostatitis; CBT, Cognitive behavioural therapy; CP/CPPS, chronic prostatitis/chronic pelvic pain syndrome; DRE, digital rectal examination; EAU, European Association of Urology; ED, erectile dysfunction; EPS, expressed prostatic secretions; GAD-7, Generalised Anxiety Disorder-7; IBS, irritable bowel syndrome; HIFU, high-intensity focused ultrasound; IIEF-5, International Index of Erectile Function; LUTS, lower urinary tract symptoms; MDT, multidisciplinary team; MRI, magnetic resonance imaging; MSU, midstream urine; NAATs, nucleic acid amplification tests; NICE, National Institute for Health and Care Excellence; NIH, National Institutes of Health (USA); NIH-CPSI, NIH Chronic Prostatitis Symptom Index; NSAID, non-steroidal anti-inflammatory drugs; OCEBM, Oxford Centre for Evidence-based Medicine; PDE5, phosphodiesterase type 5; PERG, Prostatitis Expert Reference Group; PHQ, Patient Health Questionnaire; QoL, quality of life; PSA, prostate specific antigen; RCT, randomised controlled trial; SHIM, Sexual Health Inventory for Men; SNRI, serotonin-norepinephrine reuptake inhibitor; STI, sexually transmitted infection; TENS, transcutaneous electrical nerve stimulation; TUNA, transurethral needle ablation; TURP, transurethral resection of the prostate; UPOINT, Urinary, Psychosocial, Organ-specific, Infection, Neurological/systemic, and Tenderness; UTI, urinary tract infection; VB, voided bladder.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1 Prostatitis Expert Reference Group Members.
Appendix S2 Guidelines and patient information.
Appendix S3 Literature review protocol.
Appendix S4 Chronic prostatitis/chronic pelvic pain Delphi survey.