Diagnosis and treatment of chronic bacterial prostatitis (CBP) and chronic prostatitis (CP) /chronic pelvic pain syndrome (CPPS): a consensus guideline

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Foreword

This document provides a 'quick reference guide' of the guideline and complements, but does not replace, the full guideline document. The full version of the guideline, which contains details about the methods and a description of the evidence base used to inform the treatment recommendations made, can be found at **prostatecanceruk.org/prostatitisguideline**. This quick reference guide includes the following content:

- **Introduction** – an overview of the guideline population and objectives.
- **Priorities for implementation** – an overview of the main priorities for implementation for the diagnosis and treatment of chronic bacterial prostatitis (CBP) and chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS).
- **Treatment algorithm for CBP and CP/CPPS patients** – a flow diagram 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 a Delphi panel process and consensus obtained from members of the guideline development group.
- **Table 1 – Clinical assessment and diagnosis:** a summary of physical examinations and investigations to consider during the clinical assessment of CBP and CP/CPPS.
- **Table 2 – Antibiotic treatment options to consider for the treatment of CBP**
- **Table 3 – Antineuropathic treatment options to consider for the treatment of CBP and CP/CPPS**
- **Research recommendations** – areas for potential further research.

Introduction

Overview

CBP and 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]. The main four symptom domains of CBP and CP/CPPS are urogenital pain, lower urinary tract symptoms (LUTS), psychological issues and sexual dysfunction[3]. The most common presentation of CBP is recurrent urinary tract infection (UTI), whereas pain is a predominant symptom of both CBP and CP/CPPS[3,4]. CBP and CP/CPPS also have a significant impact on patients' quality of life (QoL)[5] and present diagnostic and therapeutic challenges for physicians.

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 (National Institutes of Health [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.

Guideline population

This guideline only covers symptomatic, chronic forms of prostatitis; that is, CBP (NIH category II) and CP/CPPS (NIH category III). The patient populations under the NIH classification categories I (acute bacterial prostatitis) and IV (asymptomatic inflammatory prostatitis) were, thus, 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[6-9].

Priorities for implementation

In addition to the main treatment recommendations made in the full guideline document, which can be found on the Prostate Cancer UK website, the PERG concluded the following areas are 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.

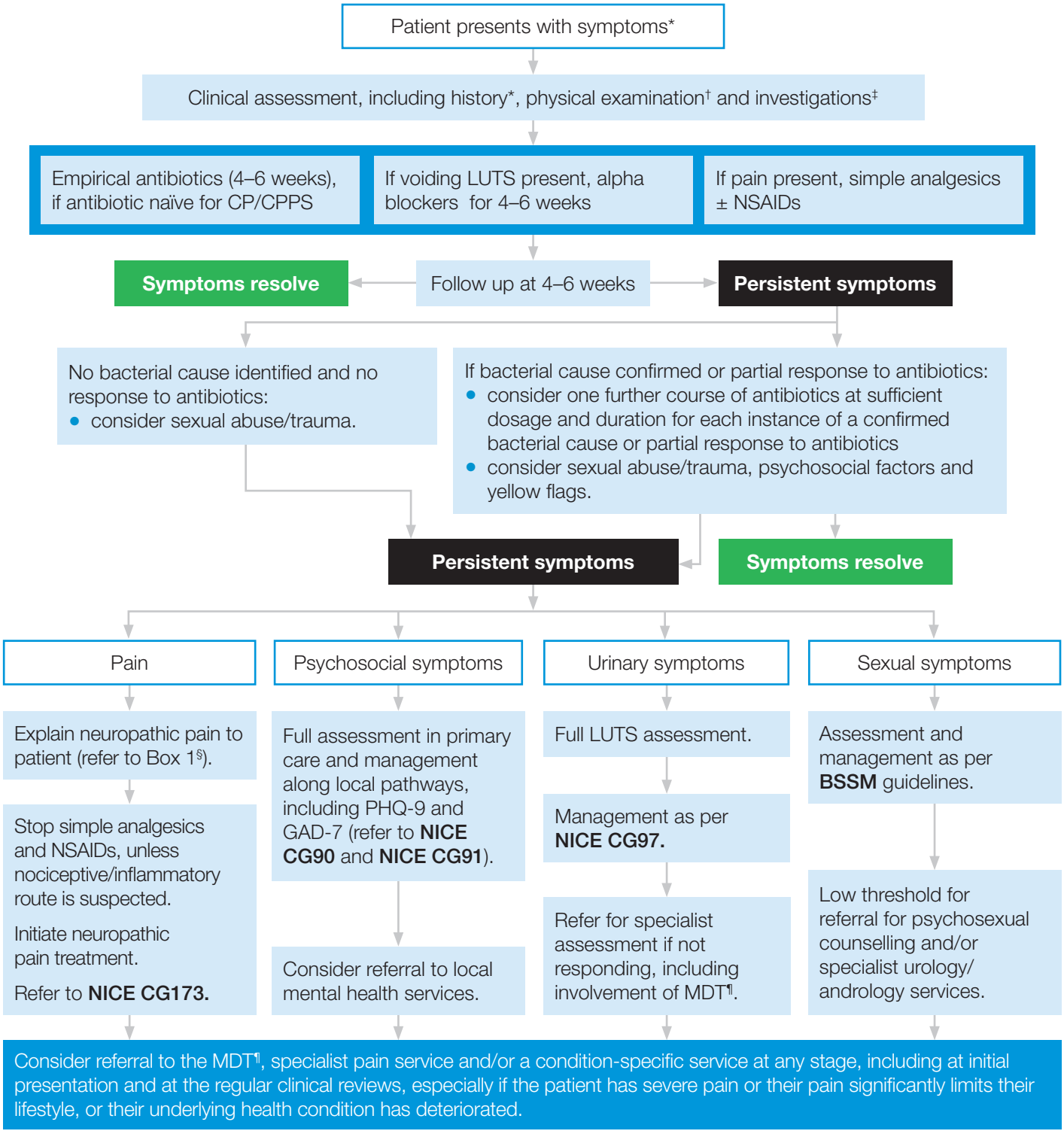
3. Early use of antineuropathic pain medication should be considered for all CBP and CP/CPPS patients refractory to initial treatments. If neuropathic pain is suspected, ensure a quick referral to the MDT, which includes pain specialists.

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.

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 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 1 can be found in the full version of the guideline: prostatecanceruk.org/prostatitisguideline

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

Table I. Summary of physical examinations and investigations

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	✓	✓	✓	
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 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[8], Map of Medicine. Prostatitis – Secondary Care, January 2014[9], Nickel et al, 2003[10] 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.

Table 2. 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[11], the British National Formulary[12] and PERG expert consensus.

Abbreviations: **bd** = twice-daily; **28/7**= seven days a week for four weeks.

Table 3. 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[12] and PERG expert consensus.

Abbreviations: **bd** = twice-daily; **GI** = gastrointestinal; **od** = once-daily; **SNRIs** = serotonin-norepinephrine reuptake inhibitors; **tds** = three times daily.

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.

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Updating the guideline

This guideline was issued in 2014 and will be considered for review in three years, 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.

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