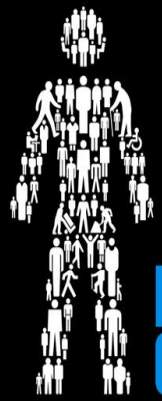
Prostatitis – management in primary care



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What is Prostatitis?????

What is prostatitis?

- Poorly understood
- Range of presentations and causes
- Prostatitis suggests inflammation of the prostate
  - **Acute** (acute prostatitis) - commonly due to infection
  - Persistent or relapsing **chronic** prostatitis (chronic pelvic pain syndrome)

> Little more is known about prostatitis than was reported by Hugh Hampton Young and associates in 1906.
> Stamey 1981

> Chronic prostatitis is a wastebasket of clinical ignorance.
> Stamey 1980

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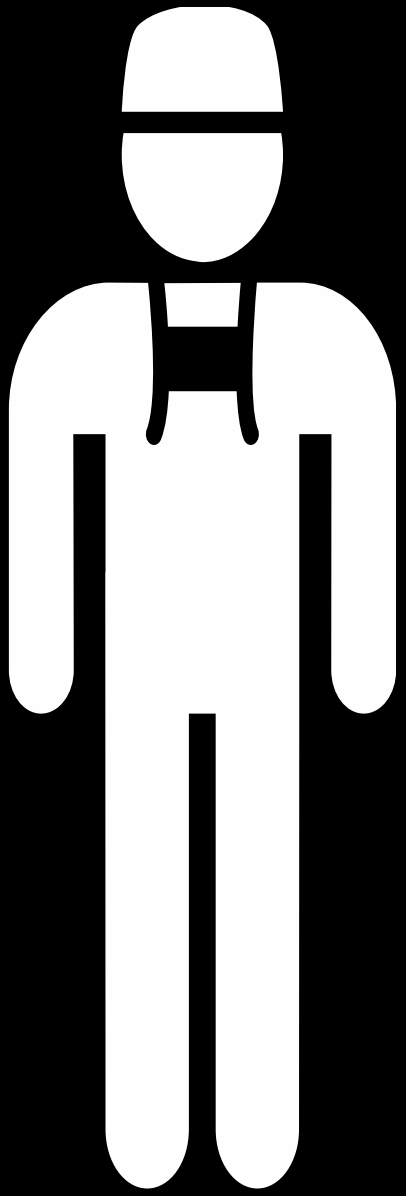
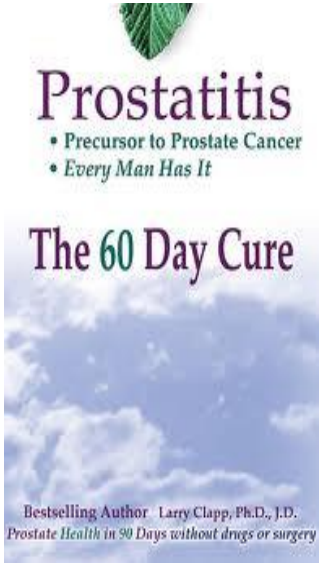
Most urologists freely acknowledge that they would be happy never to see another patient with prostatitis in their office again; others simply refuse to see these patients. Many ignore the real issue, dispensing their ‘antibiotic of the month’, and quickly discharge the patients, hoping that, if they ignore them, they will not return. This approach has resulted in frustration and even anger on the part of the patients as they either shop around for a compassionate urologist or suffer without help from the established medical community…

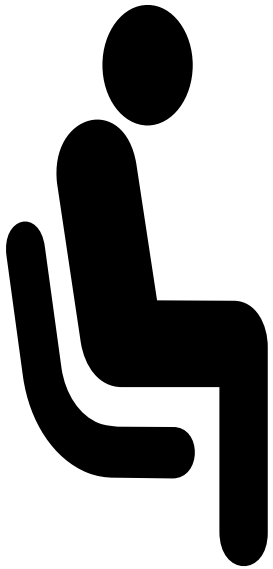
J. Curtis Nickel 1998

Nickel JC. Prostatitis: myths and realities. Urology 1998;51:362–6



Chronic prostatitis – desperate measures…





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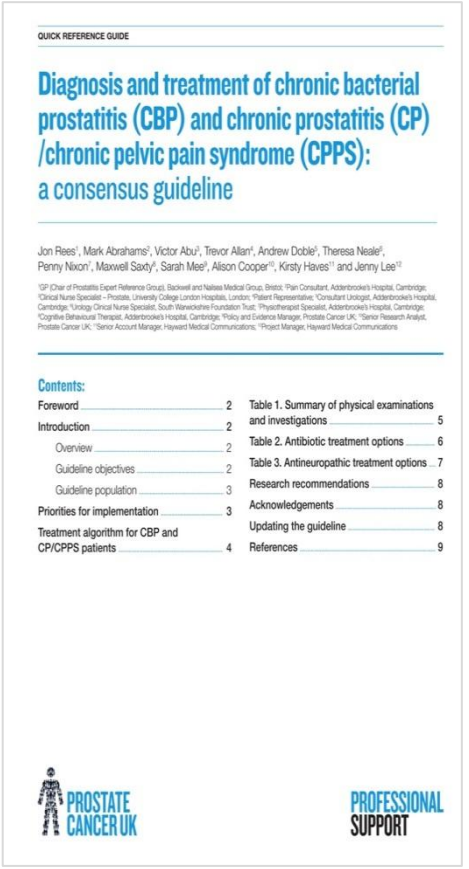
Prostatitis Expert Reference Group (PERG)

- **Primary objective:**
  - Improve patient care

- **Supporting objectives:**
  - Provide guidance to clinicians treating prostatitis, both in primary and secondary care
  - Improve awareness of the signs and symptoms of prostatitis
  - To promote the efficient sharing of care between primary and secondary care



QUICK REFERENCE GUIDE

Diagnosis and treatment of chronic bacterial prostatitis (CBP) and chronic prostatitis (CP) /chronic pelvic pain syndrome (CPPS): 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 Hayes[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

Contents:

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Prostatitis – a classification

US NIH classification:

- I: Acute bacterial prostatitis
- II: Chronic bacterial prostatitis

  (I & II account for <5% of all prostatitis diagnoses)
- **III: Chronic prostatitis/chronic pelvic pain syndrome (CPPS)**

  (>95% of prostatitis diagnoses)
- IV: Asymptomatic inflammatory prostatitis

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Acute prostatitis - diagnosis

Rarely encountered in primary care

- Usually spread from bladder/urethra/epididymis
- Patient often significantly unwell
  - high fever
  - urinary voiding symptoms (dysuria, frequency, urgency)
  - intense local pain
  - systemic features
  - retention (secondary to prostatic oedema)
- Prostate tender++ on examination – ‘boggy’
- Urine dip – leucocytes / blood positive

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Acute prostatitis - management

- Oral antibiotics – e.g. Ciprofloxacin 500mg bd for 28 days, Trimethoprim 200mg bd for 28 days if quinolone intolerant
- Analgesia & hydration
- Stool softener if defecation painful
- Early review – admit if inadequate response
- If respond well will need routine urology referral

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Chronic bacterial prostatitis

Definition: “chronic bacterial infection of the prostate (with or without symptoms of prostatitis) with a history of recurrent UTI...”

Clinical features:

- Recurrent/relapsing UTI/Urethritis/Epididymitis
- GU/pelvic pain during flare up
- Asymptomatic/mild pelvic pain/storage symptoms between episodes
- Diffusely tender prostate during episode

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CBP – diagnosis & management

- Urine dip/MSU
- Ultrasound to exclude urinary tract abnormality
- Consider flows/urodynamics
- Antibiotic – quinolone for 28 days first line
- Alpha blocker – may help alongside antibiotic
- High risk of recurrence – likely to need urological referral

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Chronic Prostatitis or Chronic Pelvic Pain Syndrome (CPPS)

- Urological heart sink
- Difficult condition for patients and doctors alike
- Symptoms can persist or fluctuate for many years
- Common - 2-14% lifetime prevalence

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Why ‘CPPS’?

While some of the symptoms experienced by men with CP/CPPS do originate from the prostate, it is increasingly understood that many of the symptoms do not, and are generated by other structures within the pelvis, or by neuropathic mechanisms within the sensory nervous system. It is for this reason that the term Chronic Pelvic Pain Syndrome (CPPS) is used, to emphasise that the prostate may not be to blame and that a more holistic approach to managing patients with these symptoms is required.

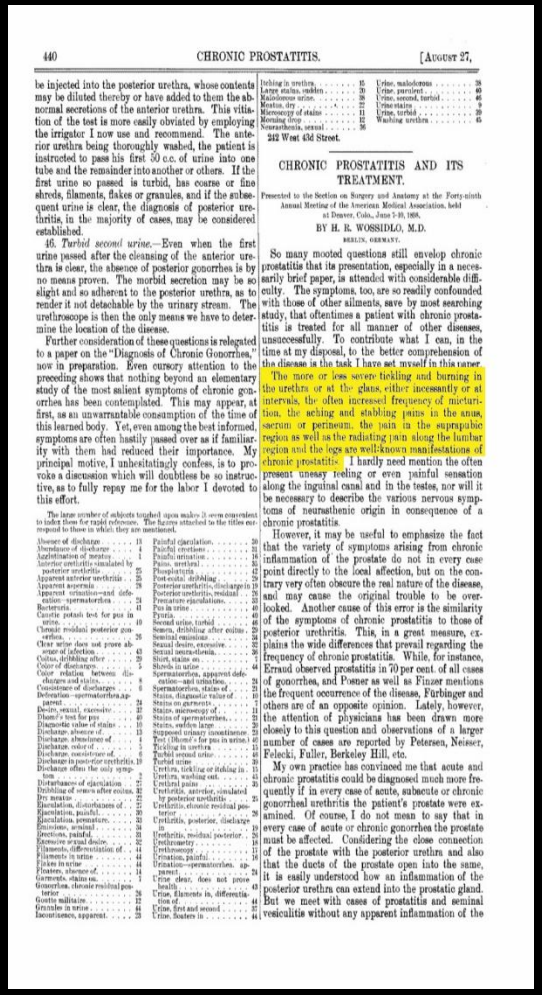
Chronic Prostatitis JAMA 1898

“

The more or less severe tickling and burning in the urethra or at the glans, either incessantly or at intervals, the often increased frequency of micturition, the aching and stabbing pains in the anus, sacrum or perineum, the pain in the suprapubic region as well as the radiating pain along the lumbar region and the legs are well-known manifestations of the chronic prostatitis. I hardly need mention the often…

H.R. Wossidlo M.D. 1898

Chronic prostatitis and its treatment. Presented to the Section on Surgery and Anatomy at the 49 Annual Meeting of the American Medical Association.



440 CHRONIC PROSTATITIS. [AUGUST 27,

be injected into the posterior urethra, whose contents may be diluted thereby or have added to them the abnormal secretions of the anterior urethra. This vitiation of the test is more easily obviated by employing the irrigator I now use and recommend. The anterior urethra being thoroughly washed, the patient is instructed to pass his first 50 c.c. of urine into one tube and the remainder into another or others. If the first urine so passed is turbid, has coarse or fine shreds, filaments, flakes or granules, and if the subsequent urine is clear, the diagnosis of posterior urethritis, in the majority of cases, may be considered established.

46. *Turbid second urine.*—Even when the first urine passed after the cleansing of the anterior urethra is clear, the absence of posterior gonorrhea is by no means proven. The morbid secretion may be so slight and so adherent to the posterior urethra, as to render it not detachable by the urinary stream. The urethroscope is then the only means we have to determine the location of the disease.

Further consideration of these questions is relegated to a paper on the “Diagnosis of Chronic Gonorrhea,” now in preparation. Even cursory attention to the preceding shows that nothing beyond an elementary study of the most salient symptoms of chronic gonorrhea has been contemplated. This may appear, at first, as an unwarrantable consumption of the time of this learned body. Yet, even among the best informed, symptoms are often hastily passed over as if familiarity with them had reduced their importance. My principal motive, I unhesitatingly confess, is to provoke a discussion which will doubtless be so instructive, as to fully repay me for the labor I devoted to this effort.

The large number of subjects touched upon makes it even convenient to index them for rapid reference. The figures attached to the titles correspond to those in which they are mentioned.

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242 West 43d Street.

CHRONIC PROSTATITIS AND ITS TREATMENT.

Presented to the Section on Surgery and Anatomy at the Forty-ninth Annual Meeting of the American Medical Association, held at Denver, Colo., June 7-10, 1898.

BY H. R. WOSSIDLO, M.D.

BERLIN, GERMANY.

So many mooted questions still envelop chronic prostatitis that its presentation, especially in a necessarily brief paper, is attended with considerable difficulty. The symptoms, too, are so readily confounded with those of other ailments, save by most searching study, that oftentimes a patient with chronic prostatitis is treated for all manner of other diseases, unsuccessfully. To contribute what I can, in the time at my disposal, to the better comprehension of this disease is the task I have set myself in this paper.

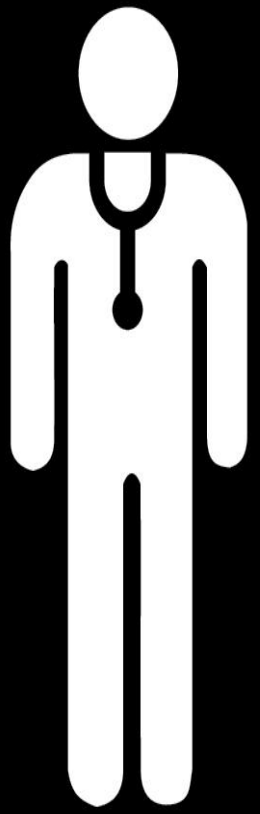
The more or less severe tickling and burning in the urethra or at the glans, either incessantly or at intervals, the often increased frequency of micturition, the aching and stabbing pains in the anus, sacrum or perineum, the pain in the suprapubic region as well as the radiating pain along the lumbar region and the legs are well-known manifestations of chronic prostatitis. I hardly need mention the often present uneasy feeling or even painful sensation along the inguinal canal and in the testes, nor will it be necessary to describe the various nervous symptoms of neurasthenic origin in consequence of a chronic prostatitis.

However, it may be useful to emphasize the fact that the variety of symptoms arising from chronic inflammation of the prostate do not in every case point directly to the local affection, but on the contrary very often obscure the real nature of the disease, and may cause the original trouble to be overlooked. Another cause of this error is the similarity of the symptoms of chronic prostatitis to those of posterior urethritis. This, in a great measure, explains the wide differences that prevail regarding the frequency of chronic prostatitis. While, for instance, Ernaud observed prostatitis in 70 per cent. of all cases of gonorrhea, and Posner as well as Finger mentions the frequent occurrence of the disease, Fürbinger and others are of an opposite opinion. Lately, however, the attention of physicians has been drawn more closely to this question and observations of a larger number of cases are reported by Petersen, Neisser, Felecki, Fuller, Berkeley Hill, etc.

My own practice has convinced me that acute and chronic prostatitis could be diagnosed much more frequently if in every case of acute, subacute or chronic gonorrheal urethritis the patient's prostate were examined. Of course, I do not mean to say that in every case of acute or chronic gonorrhea the prostate must be affected. Considering the close connection of the prostate with the posterior urethra and also that the ducts of the prostate open into the same, it is easily understood how an inflammation of the posterior urethra can extend into the prostatic gland. But we meet with cases of prostatitis and seminal vesiculitis without any apparent inflammation of the

Chronic Prostatitis JAMA 1898

I mention the great frequency of nervous troubles as a sequel of chronic prostatitis. The more or less constant uneasy or painful sensations along the genito-urinary tract constantly draw the patient's thoughts to this region. Should he then, in addition to his disagreeable sensations, observe a degree of sexual weakness, incomplete erection or premature seminal emission, our patient's spirit becomes depressed. He is constantly worrying over his illness and loses all capacity for mental or physical work. In the worst cases general nervous debility sets in, not infrequently increasing to more or less complete exhaustion. Our patients become more or less obstinate hypochondriacs. It would be impossible to go into the details…



H.R. Wossidlo M.D. 1898

Chronic prostatitis and its treatment. Presented to the Section on Surgery and Anatomy at the 49 Annual Meeting of the American Medical Association.

CP/CPPS - presentation

Suggested definition: ‘presence of typical symptoms of discomfort or pain in the genital or pelvic region for more than three months within the past six months’

- Urogenital Pain
- Lower Urinary Tract Symptoms
- Sexual Dysfunction
- Psychological Issues

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CP/CPPS: Symptoms

- **Urogenital pain**
  - Perineum
  - Suprapubic region
  - Testicles/Penis (especially penile tip pain)
  - Lower back
  - Abdomen/Inguinal region/groin
  - Rectum
  - Pain on urination
  - Functional bowel symptoms (eg, IBS)
- **Lower Urinary Tract Symptoms**
  - Voiding and/or Storage LUTS
  - Urethral burning during, and independent of, micturition
  - Recurrent UTI (more applicable to CBP)

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CP/CPPS: Symptoms (cont.)

- **Sexual Dysfunction**
  - Erectile dysfunction
  - Ejaculatory dysfunction/pain
  - Decreased libido
  - Haematospermia (blood in semen)
- **Psychological Issues**
  - Anxiety
  - Depression
  - QoL impact

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Initial assessment

NIH-CPSI

- 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)

- Urinary symptoms (seven questions, 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) 5-item questionnaire for screening/diagnosis of ED

Patient Health Questionnaire-9 (PHQ-9)
9-item questionnaire to assess the frequency of depressed mood

Generalised Anxiety Disorder-7 (GAD-7)
7-item questionnaire to assess the severity of anxiety

Summary of physical examination/investigations

Examination/Investigation	Non-specialist	Specialist	Core	Optional
Examination of abdomen, external genitalia & DRE	X	X	X	
Urine dip +/- MSU	X	X	X	
4-glass or 2-glass test		X		X
PSA	X	X	X	
STI Screen	X	X	X	
Uroflowmetry		X		X
Imaging (TRUS or MRI)		X		X
Prostate Biopsy		X		X
Urethral Swab & Culture		X		X

www.prostatecanceruk.org/prostatitisguideline

Psycho-social factors to consider when assessing men with CP/CPPS

Any pre-existing or current mental health problems?

Anxiety screening questions:

- In the last month have you often been bothered by:
  - feeling nervous, anxious or on edge?
  - not been 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?

Screening for trauma and/or abuse:

- When growing up, or more recently, have any relationships been difficult or have situations happened that you have found yourself uncomfortable with?

Life events:

- Have you recently undergone any major life events
  e.g. moving house, divorce, bereavement, change of job/career?

If "yes" to any of the above questions further questioning is required from a practitioner who is competent in mental health assessment.

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NICE Clinical Guideline 91 – Depression in adults with a chronic physical health problem (2009)

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CP/CPPS – treatment options

- Antibiotics
- Alpha-blockers
- NSAID’s
- Allopurinol
- Finasteride
- Phytotherapy
  - Cernilton
  - Quercetin
- Amitriptylline
- Gabapentin/Pregabalin

- Prostatic massage
- Pelvic floor physio
- Cognitive behavioural therapy
- Hyperthermia
- Acupuncture
- Thermotherapy
- Electromagnetic therapy
- ESWL

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Antibiotics for CP/CPPS

- Antimicrobial therapy has a moderate effect on total, pain, voiding and QoL

- Single use of antimicrobial therapy (quinolones or tetracyclines) is recommended in
  treatment-naïve patients over a minimum of six weeks with a duration of CPPS < 1 year

- Need to move away from model that CP/CPPS is an infective process & decrease
  antibiotic use.

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Antibiotic options

Antibiotic	Advantages	Considerations	PERG recommendation
Quinolones: **eg, 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, eg: 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, eg: TRIMETHOPRIM 200 mg bd 28/7
Tetracyclines: **eg, 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, eg: DOXYCYCLINE 100 mg bd 28/7
Macrolides: **eg, 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[12], the British National Formulary[24] and PERG expert

Alpha blockers for CP/CPPS

- Systematic review of eight trials (Cohen 2012)
- Among 7/8 RCTs (n= 770) comparing alpha-blockers to placebo:
  - Average NIH-CPSI **total** reduction of 4.8 (95% CI: -7.1 to -2.6)
  - Average NIH-CPSI **pain** reduction of 2.1 (95% CI: -3.1 to -1.2
  - Average NIH-CPSI **voiding** reduction of 1.1 (95% CI: -1.7 to -0.4 [7 RCTs]
  - Average NIH-CPSI **QoL** reduction of 1.4 (95% CI: -2.3 to -0.4) [7 RCTs]

- EAU guidelines for chronic pelvic pain (Feb 2012):
  - α–blockers have moderate treatment effect regarding total, pain, voiding, and QoL scores in PPS (1a) and are recommended for patients with a duration of PPS < 1 year

NSAID’s for CP/CPPS

- Limited data for use of NSAID’s
- Moderate effect on symptoms, predominantly pain
- Most beneficial during early stages of CPPS (? first six months)
- Or for acute inflammatory flare
- Try to avoid long term use due to side effect profile

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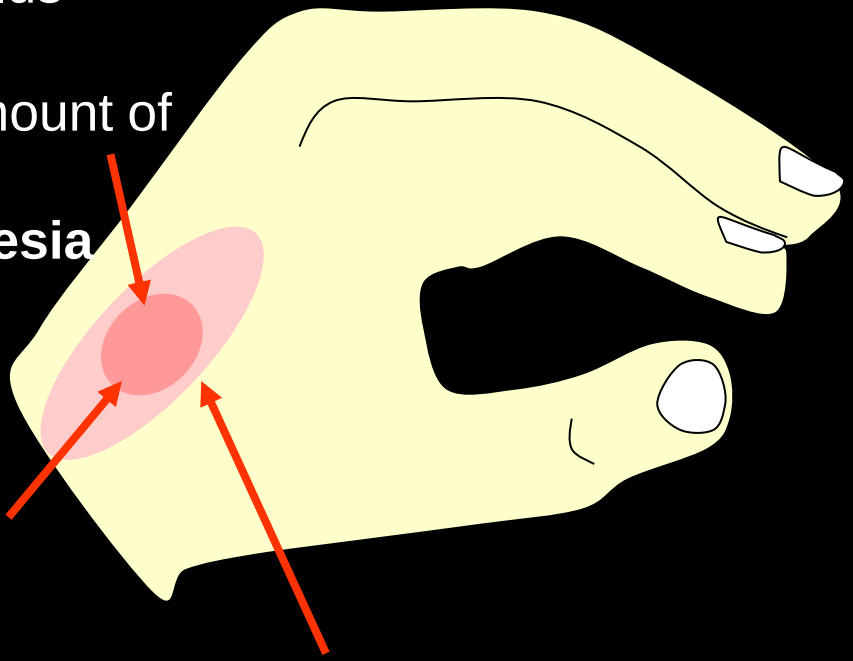
Central Sensitisation

Painful stimulus produces increased amount of pain

- **Hyperalgesia**



Non-noxious stimulus produces pain

- **Allodynia**

Expansion of painful area beyond the site of injury

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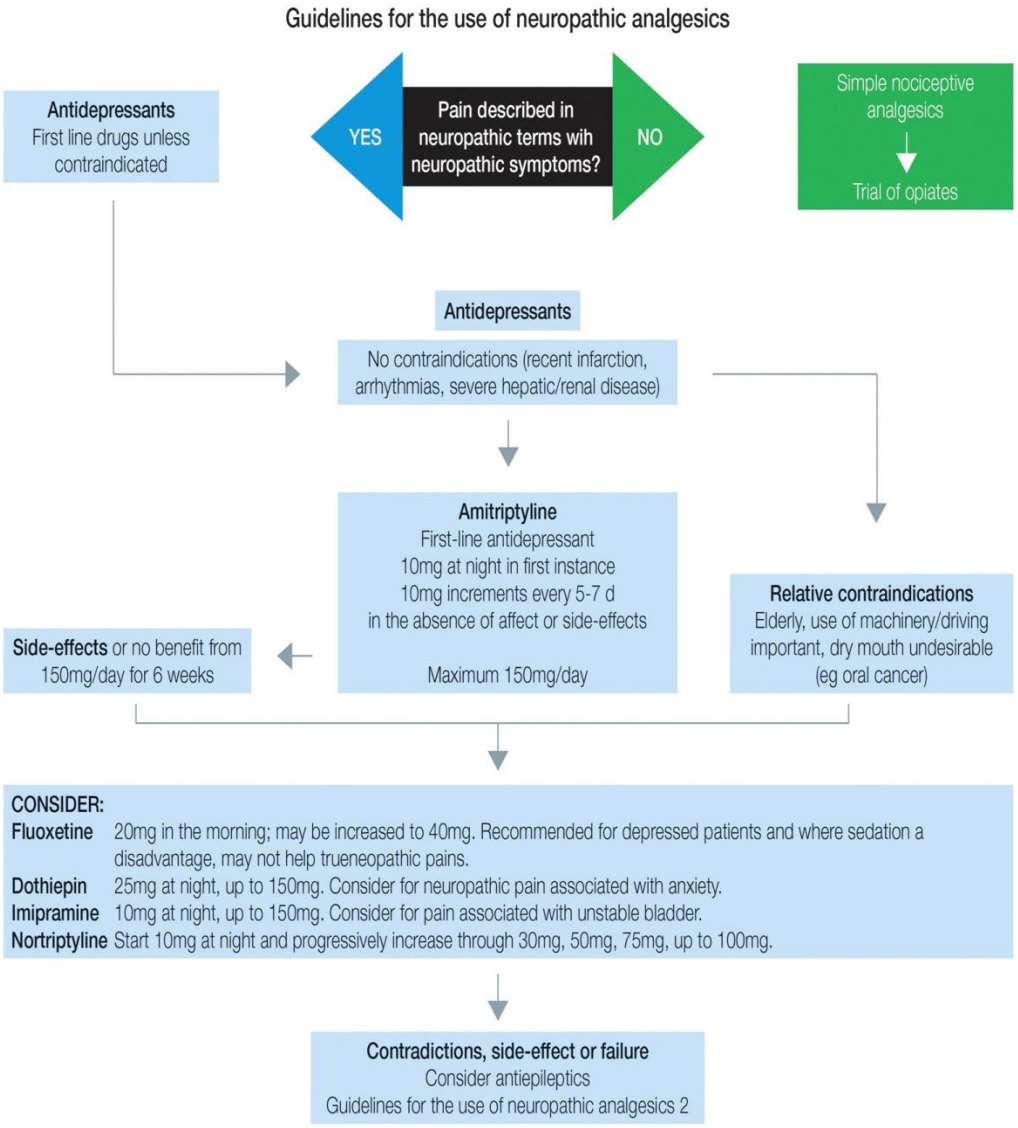
Use of neuropathic analgesics



EAU Chronic Pelvic Pain Guidelines

NICE Neuropathic pain guidelines – CG173

- Offer a choice of amitriptyline, duloxetine, gabapentin or pregabalin as initial treatment for neuropathic pain.

- If the initial treatment is not effective or is not tolerated, offer one of the remaining three drugs, and consider switching again if the second and third drugs tried are also not effective or not tolerated.

- Titrate dose to achieve therapeutic effect.

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Anti-neuropathic treatment options

Analgesic class	Drug name	Starting dose	Maintenance dose	Common adverse effects	PERG practical points
Gabapentinoids	GABAPENTIN	100–300mg at night	600mg 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	50–75mg at night	300mg bd	Dizziness, sedation, dyspepsia, dry mouth, ataxia, peripheral oedema, weight gain.	Linear pharmacokinetics .
ic antidepressants/SNRIs	AMITRIPTYLINE	10mg in evening	50–75mg in evening	Sedation, dry mouth, blurred vision, urinary retention, constipation, postural hypotension, weight gain.	Many patients obtain pain relief at lower dose.
	DULOXETINE	30mg in evening (or in morning, if insomnia)	60–120mg od	Nausea, sedation, insomnia,	Less sedating. May cause insomnia in some

Specialist Physiotherapy

- Studies have shown that the symptoms of CP/CPPS may be the result of physical dysfunction, such as abnormal pelvic muscle spasm and muscle tenderness.
- Majority of evidence for treating CP/CPPS with specialist physiotherapy is derived from small proof-of-principle or pilot studies.
- Important to exclude underlying causes for symptoms e.g. infection, prostate cancer etc prior to physiotherapy referral.

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- Multiple treatment options (Level 5 evidence):
  - Pelvic floor re-education
  - Local pelvic floor relaxation
  - Biofeedback
  - General relaxation
  - Deep relaxation/mindfulness
  - Trigger point release
  - Myofascial release
  - Daily exercise encouraged for pain management
  - TENS
  - Acupuncture for trigger point release and pain management
  - Bladder retraining

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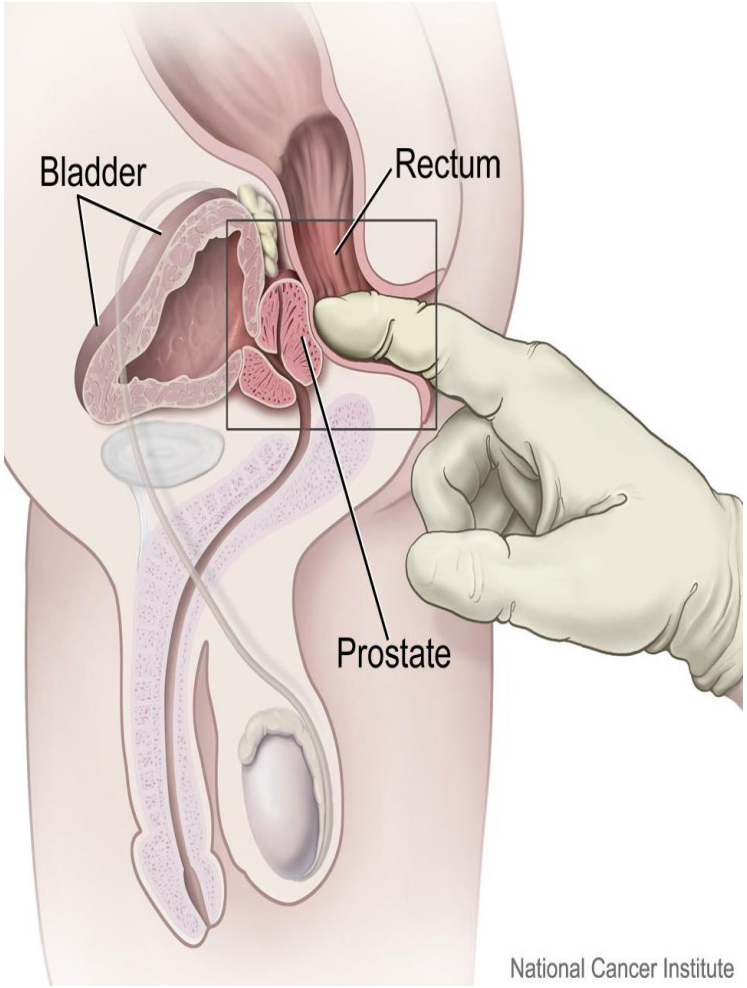
CP/CPPS - phytotherapy

- Pollen extract: Cernilton
  - 1 study suggesting 78% of men taking tds had benefit
- Flavonoids: Quercetin
  - 1 prospective double blind RCT – 30 men
  - Significant improvement vs placebo
- Saw palmetto
  - Poor evidence base for benefit in chronic prostatitis
- 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).

Prostatic Massage

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).



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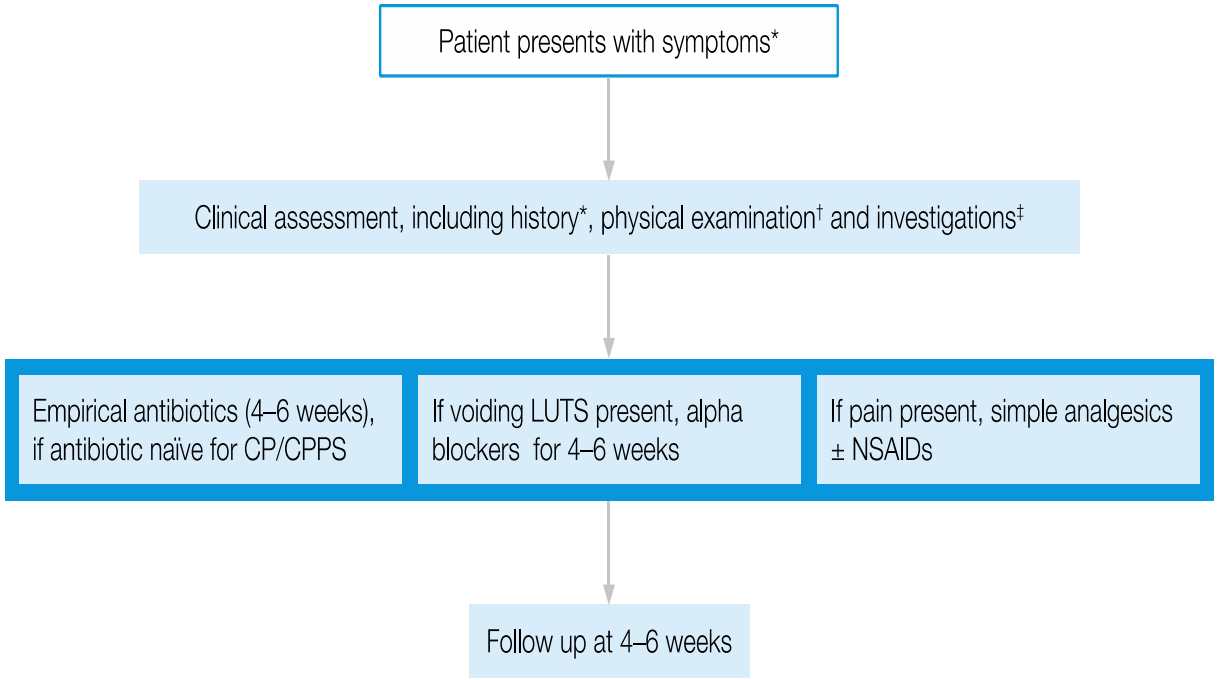
Treatment algorithm



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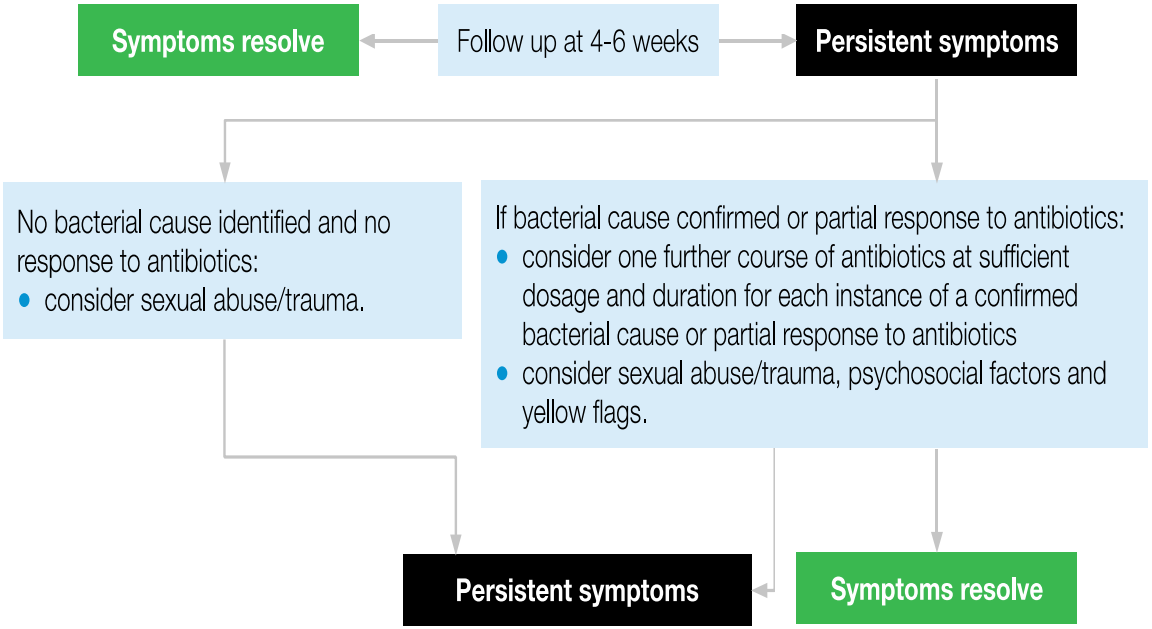

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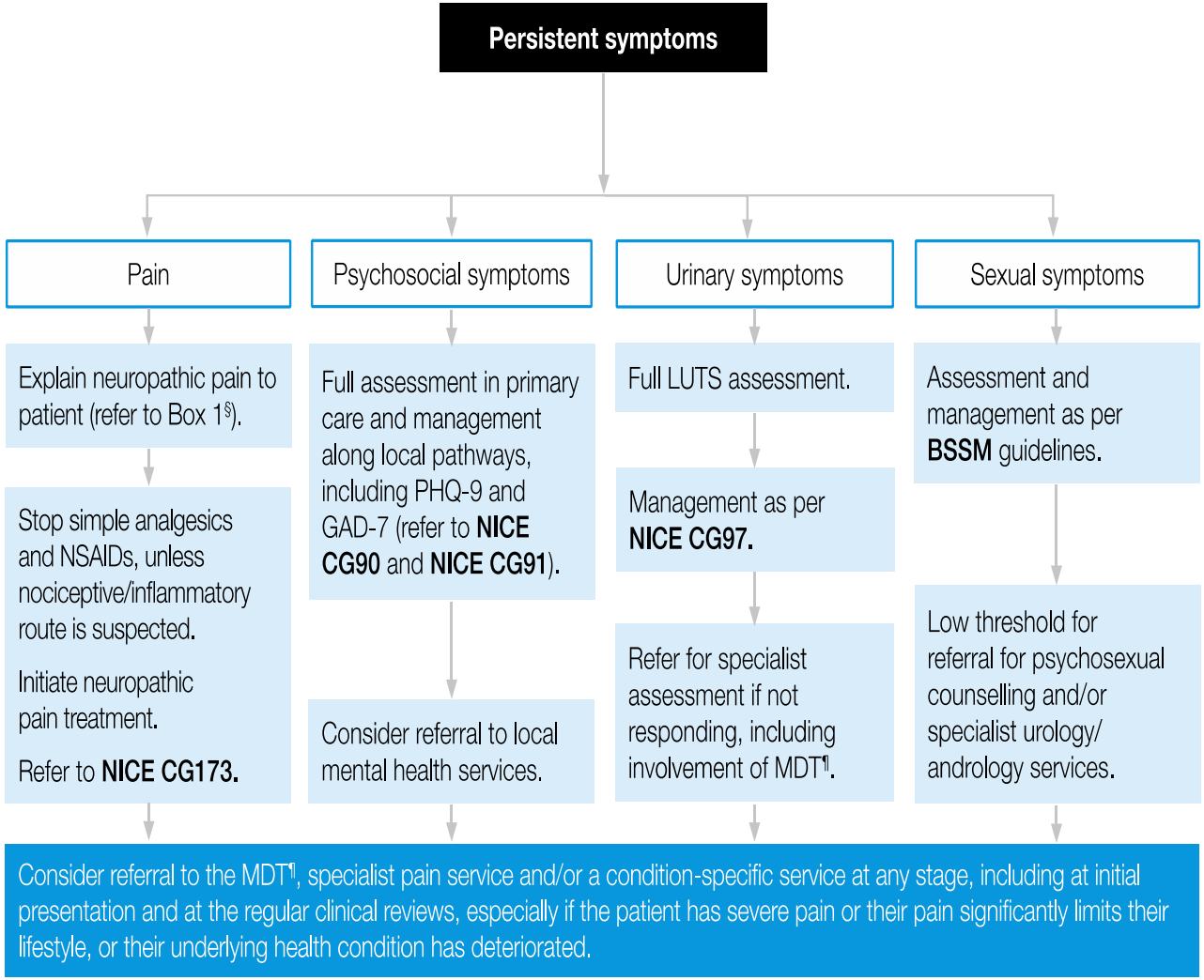

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Priorities for implementation

- 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.

- 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.

- 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.

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Priorities for implementation (2)

- 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.

- 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.

- 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.

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Research Recommendations

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

Research Recommendations (2)

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

Chronic prostatitis

- Normal two year course
- 33% no symptoms at one year
- 33% moderate/marked improvement at two years
- Prognosis worse in those with:
  - Severe symptoms
  - Anxiety/depression
  - Ejaculatory pain

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Thank you

- PERG Guideline: available to download at: www.prostatecanceruk.org/prostatitisguideline
- Prostate Cancer UK website & telephone support service www.prostatecanceruk.org
- Guideline endorsed by BASHH, BAUS, BAUN, NICE CKS
- Summary published in British Journal of Urology International 2015[1]

1: Rees J et al, BJU Int 2015; 116 (4): 509-525