ClinicalEvidence

Chronic prostatitis

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Bradley A Erickson, Brian V Le and Anthony J Schaeffer

ABSTRACT

INTRODUCTION: Chronic prostatitis can cause pain and urinary symptoms, and usually occurs without positive bacterial cultures from prostatic secretions (known as chronic abacterial prostatitis or chronic pelvic pain syndrome, CP/CPPS). Bacterial infection can result from urinary tract instrumentation, but the cause and natural history of CP/CPPS are unknown. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of treatments for chronic bacterial prostatitis? What are the effects of treatments for chronic abacterial prostatitis/chronic pelvic pain syndrome? We searched: Medline, Embase, The Cochrane Library and other important databases up to August 2007 (BMJ Clinical Evidence reviews are updated periodically, please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 30 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review we present information relating to the effectiveness and safety of the following interventions: 5 alpha-reductase inhibitors, allopurinol, alpha-blockers, biofeedback, local injections of antimicrobial drugs, mepartricin, non-steroidal anti-inflammatory drugs, oral antimicrobial drugs, pentosan polysulfate, prostatic massage, quercetin, radical prostatectomy, sitz baths, transurethral microwave thermotherapy, and transurethral resection.

QUESTIONS

What are the effects of treatments for chronic bacterial prostatitis? . . . 3

What are the effects of treatments for chronic abacterial prostatitis/chronic pelvic pain syndrome? . . . 6

INTERVENTIONS

CHRONIC BACTERIAL PROSTATITIS

Likely to be beneficial

Oral antimicrobial drugs for chronic bacterial prostatitis . . . 3

Unknown effectiveness

Alpha-blockers for chronic bacterial prostatitis . . . 4

Local injection of antimicrobial drugs . . . 5

NSAIDs for chronic bacterial prostatitis . . . 6

Radical prostatectomy . . . 6

TURP . . . 6

CHRONIC ABACTERIAL PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME (CP/CPPS)

Likely to be beneficial

Alpha-blockers for chronic abacterial prostatitis/chronic pelvic pain syndrome . . . 6

Unknown effectiveness

5 alpha-reductase inhibitors . . . 8

Allopurinol . . . 9

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Unlikely to be beneficial

Oral antimicrobial drugs for chronic abacterial prostatitis/chronic pelvic pain syndrome . . . 12

Prostatic massage . . . 12

Key points

- Chronic prostatitis can cause pain and urinary symptoms, and usually occurs without positive bacterial cultures from prostatic secretions (known as chronic abacterial prostatitis or chronic pelvic pain syndrome, CP/CPPS).

  Bacterial infection can result from urinary tract instrumentation, but the cause and natural history of CP/CPPS are unknown.

- Chronic bacterial prostatitis has identifiable virulent micro-organisms in prostatic secretions.

  Oral antimicrobial drugs are likely to be beneficial, although studies comparing them with placebo or no treatment have not been found.

  Clinical success rates from oral antimicrobials have reached about 70–90% at 6 months in studies comparing different regimens.

  Trimethoprim–sulfamethoxazole (co-trimoxazole) and quinolones are most commonly used and seem the most beneficial.

  Alpha-blockers may reduce symptoms and reduce recurrence of chronic prostatitis if added to antimicrobial treatment.

We don't know whether local injections of antimicrobial drugs, NSAIDs, transurethral resection, or radical prostatectomy improve symptoms compared with no treatment.

- Effective treatment regimens for CP/CPPS remain to be defined, and strategies are based on symptomatic control and anxiety relief.

  Alpha-blockers may improve quality of life and symptoms compared with no treatment.

  Oral antimicrobial drugs have not been shown to improve symptoms.

  We don't know whether 5 alpha-reductase inhibitors, NSAIDs, pentosan polysulfate, allopurinol, transurethral microwave thermotherapy, prostatic massage, Sitz baths, biofeedback, mepartricin, or quercetin reduce symptoms in men with CP/CPPS.

DEFINITION

Chronic bacterial prostatitis is characterised by a positive culture of expressed prostatic secretions. It may cause symptoms such as suprapubic, lower back, or perineal pain, with or without mild urgency and increased frequency of urination, and dysuria, and may be associated with recurrent UTI. However, it may also be asymptomatic between acute episodes/exacerbations. **Chronic abacterial prostatitis/chronic pelvic pain syndrome (CP/CPPS)**, is characterised by pelvic or perineal pain in the absence of pathogenic bacteria in expressed prostatic secretions. It is often associated with irritative and obstructive voiding symptoms including urgency, frequency, hesitancy, and poor interrupted flow. Symptoms can also include: pain in the suprapubic region, lower back, penis, testes, or scrotum; and painful ejaculation. CP/CPPS may be inflammatory (white cells present in prostatic secretions) or non-inflammatory (white cells absent in prostatic secretions). [1] A classification system for the prostatitis syndromes has been developed by the National Institutes of Health (NIH). [2]

INCIDENCE/ PREVALENCE

One community-based study in the USA (cohort of 2115 men aged 40–79 years) estimated that 9% of men have a diagnosis of prostatitis at any one time. [3] Another observational study found that, in men presenting with genito-urinary symptoms, 8% of those presenting to urologists and 1% of those presenting to primary-care physicians were diagnosed as having chronic prostatitis. [4] Most cases of chronic prostatitis are abacterial. Chronic bacterial prostatitis, although easy to diagnose, is rare.

AETIOLOGY/ RISK FACTORS

Organisms commonly implicated in bacterial prostatitis include *Escherichia coli*, other Gram-negative enterobacteriaceae, occasionally *Pseudomonas* species and, rarely, Gram-positive enterococci. Risk factors for bacterial prostatitis include urethral catheterisation or instrumentation, condom drainage, dysfunctional voiding (high-pressure urination), and unprotected anal intercourse. The cause of CP/CPPS is unclear, although it has been suggested that it may be caused by undocumented infections with *Chlamydia trachomatis*, [5] *Ureaplasma urealyticum*, [6] *Mycoplasma hominis*, [7] and *Trichomonas vaginalis*. [8] Viruses, [9] [10] *Candida* (in immunosuppressed people), [11] and parasites [12] have also rarely been implicated. Non-infectious factors might also be involved, including inflammation, [13] autoimmunity, [14] hormonal imbalances, [15] pelvic floor tension myalgia, [16] intraprostatic urinary reflux, [17] and psychological disturbances. [18] In one case control study (463 men with CP/CPPS, 121 asymptomatic age-matched controls), when compared with controls, men with CP/CPPS reported a significantly higher lifetime prevalence of non-specific urethritis (12% with CP/CPPS *v* 4% with no CP/CPPS; P = 0.008), CVD (11% with CP/CPPS *v* 2% with no CP/CPPS; P = 0.004), neurological disease (41% with CP/CPPS *v* 14% with no CP/CPPS; P less than 0.001), psychiatric conditions (29% with CP/CPPS *v* 11% with no CP/CPPS; P less than 0.001), and haematopoietic, lymphatic, or infectious disease (41% with CP/CPPS *v* 20% with no CP/CPPS; P less than 0.001). [19] Further studies are necessary to determine whether these factors play a role in the pathogenesis of CP/CPPS. [19]

PROGNOSIS

The natural history of untreated chronic bacterial and abacterial prostatitis/chronic pelvic pain syndrome (CP/CPPS) remains ill-defined. Chronic bacterial prostatitis may cause recurrent UTI in men whereas CP/CPPS does not. [20] Several investigators have reported an association between chronic bacterial prostatitis, CP/CPPS, and infertility. [21] One study found that CP/CPPS had an impact on quality of life similar to that of angina, Crohn's disease, or a previous MI. [22]

AIMS OF INTERVENTION

To relieve symptoms and eliminate infection where present, with minimum adverse effects.

OUTCOMES

Symptom improvement (symptom scores, bother scores); quality of life; urodynamics; rates of bacteriological cure (clearance of previously documented organisms from prostatic secretions); adverse effects of treatment.

METHODS

BMJ Clinical Evidence search August 2007. The following databases were used to identify studies for this systematic review: Medline 1966 to August 2007, Embase 1980 to August 2007, and The

Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Clinical Trials 2007, Issue 3. Additional searches were carried out using these websites: NHS Centre for Reviews and Dissemination (CRD) — for Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA), Turning Research into Practice (TRIP), and NICE. We also searched for retractions of studies included in the review. Abstracts of the studies retrieved from the initial search were assessed by an information specialist. Selected studies were then sent to the author for additional assessment, using pre-determined criteria to identify relevant studies. Study design criteria for inclusion in this review were: published systematic reviews and RCTs in any language. RCTs had to be at least single-blinded where possible to blind, and contain 20 or more individuals, of whom more than 80% were followed up. There was no minimum length of follow-up required to include studies. We excluded all studies described as "open", "open label", or not blinded unless blinding was impossible. In addition, we use a regular surveillance protocol to capture harms alerts from organisations such as the FDA and the UK Medicines and Healthcare products Regulatory Agency (MHRA), which are added to the reviews as required. We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 15).

QUESTION What are the effects of treatments for chronic bacterial prostatitis?

OPTION ORAL ANTIMICROBIAL DRUGS FOR CHRONIC BACTERIAL PROSTATITIS

Symptom improvement
Oral antimicrobial drugs compared with each other Lomefloxacin or levofloxacin are as effective as ciprofloxacin at achieving clinical success rates (defined as complete resolution of symptoms, improvement in symptoms, or clear improvement without need for additional antimicrobial drugs) at 6 months (moderate-quality evidence).

Cure rates
Oral antimicrobial drugs compared with each other Lomefloxacin or levofloxacin are as effective as ciprofloxacin at increasing bacteriological cure rates at 6 months, and prulifloxacin and levofloxacin are equally effective at increasing microbiological eradication rates at 6 months in men with chronic bacterial prostatitis (moderate-quality evidence).

Note
We found no direct information about whether oral antimicrobial drugs are better than no active treatment or no antimicrobial treatment in men with chronic bacterial prostatitis.

For GRADE evaluation of interventions for chronic prostatitis, see table, p 15 .

Benefits:

Oral antimicrobial drugs versus placebo or no antimicrobial drugs:
We found no systematic review or RCTs.

Oral antimicrobial drugs versus each other:
We found no systematic review but found three RCTs. [23] [24] [25] The first RCT (182 men) compared lomefloxacin 400 mg daily versus ciprofloxacin 500 mg twice daily for 4 weeks. [23] It found no significant difference after 6 months between lomefloxacin and ciprofloxacin in rates of clinical success (61/93 [67%] with lomefloxacin *v* 64/89 [72%] with ciprofloxacin; difference –5%, 95% CI –23.6% to +6.0%, P = 0.158) or bacteriological cure (49/93 [53%] with lomefloxacin *v* 54/89 [61%] with ciprofloxacin; difference –8%, 95% CI –26.0% to +6.0%, P = 0.618). Clinical success was defined as clinical cure (baseline symptoms completely resolved) or improvement (symptoms improved but not completely resolved). The second RCT (377 men) compared levofloxacin 500 mg daily versus ciprofloxacin 500 mg twice daily for 28 days. [24] It found no significant difference in rates of clinical success after 6 months between levofloxacin and ciprofloxacin (defined as complete resolution of symptoms or clear improvement without need for additional antimicrobial drugs: 102/136 [75%] with levofloxacin *v* 91/125 [73%] with ciprofloxacin; difference –2.2%, 95% CI –13.3% to +8.9%) or bacteriological cure (102/136 [75%] with levofloxacin *v* 96/125 [77%] with ciprofloxacin; difference –1.8%, 95% CI –9.0% to +12.6%, P values reported as not significant). The third RCT (96 men with chronic bacterial prostatitis) compared a newer fluoroquinolone (prulifloxacin 600 mg daily) with levofloxacin (500 mg daily) for 4 weeks. The RCT found no significant difference in microbiological eradication rates at 6 months after treatment completion, as determined by follow-up Meares–Stamey tests, (32/44 [73%] with prulifloxacin *v* 32/45 [71%] with levofloxacin; P = 0.86) or in total National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) mean score decreases (10.75 [range 17.22 to 6.47] with prulifloxacin *v* 10.73 [range 17.33 to 6.6] with levofloxacin; P = 0.98). [25]

Harms:

Oral antimicrobial drugs versus placebo or no antimicrobial drugs:
We found no systematic review or RCTs.

Oral antimicrobial drugs versus each other:
The first RCT comparing lomefloxacin versus ciprofloxacin found that the most common adverse effects with both treatments were gastrointestinal disorders (5/93 [5%] with lomefloxacin *v* 8/89 [9%] with ciprofloxacin; P value not reported). [23] Adverse effects caused the premature withdrawal of a similar proportion of men on both treatments (5/93 [5%] with lomefloxacin *v* 4/89 [4%] with ciprofloxacin; P value not reported). [23] The second RCT found similar proportions of men reporting at least one treatment-related adverse event with ciprofloxacin and levofloxacin (87/197 [44%] with levofloxacin *v* 67/180 [37%] with ciprofloxacin; P value not reported). [24] It found that the most common adverse effects with both treatments were gastrointestinal disturbances (19% with levofloxacin *v* 17% with ciprofloxacin; P value not reported). The third RCT reported a similar number of people with adverse events in the two treatment groups (8/44 [18%] for prulifloxacin *v* 10/45 [22%] for levofloxacin; P = 0.79). Events were mostly minor in nature (diarrhoea, skin rash, gastric pain, headache, nausea), although one person in the levofloxacin group withdrew from the study owing to gastric pain. [25]

Comment:

We found data from retrospective case series about the bacteriological cure rates of different antimicrobials. [26] [27] [28] These data do not compare antimicrobial drugs versus placebo, no treatment, or other treatments.

Trimethoprim–sulfamethoxazole (co-trimoxazole):
One non-systematic review identified eight retrospective case series in 1140 men with bacteriologically confirmed prostatitis treated with trimethoprim–sulfamethoxazole (trimethoprim 160 mg plus sulfamethoxazole 800 mg twice daily for 10–140 days). [26] The studies reported cure rates of 0–71%. Over 30% of men were cured when treated for at least 90 days. The review did not report on adverse effects.

Quinolones:
One non-systematic review summarised three retrospective case series in 106 men treated with norfloxacin (400 mg twice daily for 10, 28, and 174 days). [27] The studies reported cure rates of 64–88%.

Amoxicillin/clavulanic acid (co-amoxiclav) and clindamycin:
One case series included 50 men resistant to empirical treatment with quinolones. [28] The expressed prostatic secretions from 24 of these men exhibited high colony counts of Gram-positive and Gram-negative anaerobic bacteria, either alone (18 men) or in combination with aerobic bacteria (6 men). After treatment with either amoxicillin/clavulanic acid or clindamycin for 3–6 weeks, all men had a decrease or total elimination of symptoms, and no anaerobic bacteria were detected in prostatic secretions. [28] Higher cure rates with quinolones may be explained by greater penetration into the prostate. [29] We reviewed only studies that used standard methods to localise infection to the prostate. [30]

Clinical guide:
Most clinicians agree that antimicrobial drugs are the preferred treatment for chronic bacterial prostatitis. However, if symptoms do not improve after eradication of bacteria, alternative treatments should be investigated.

OPTION ALPHA-BLOCKERS FOR CHRONIC BACTERIAL PROSTATITIS

Recurrence rates
Alpha-blockers plus antimicrobial drugs compared with antimicrobial drugs alone Alpha-blockers (terazosin, alfuzosin) plus antimicrobial drugs may be more effective at reducing recurrence rates (assessed by culture or expressed prostatic secretion) in men with chronic bacterial prostatitis compared with antimicrobial drugs alone (low-quality evidence).

Note
We found no direct evidence whether alpha-blockers are better than no active treatment in men with chronic bacterial prostatitis.

For GRADE evaluation of interventions for chronic prostatitis, see table, p 15 .

Benefits:

Alpha-blockers versus placebo:
We found no systematic review or RCTs.

Alpha-blockers plus antimicrobial drugs versus antimicrobial drugs alone:
We found one RCT (64 men with bacterial prostatitis; mean age 48 years) comparing alpha-blockers (terazosin 1–2 mg/day, or terazosin 2.5 mg/day, or alfuzosin 2.5 mg once or twice daily) plus antimicrobial drugs versus antimicrobial drugs alone. [31] It found that alpha-blockers plus

antimicrobial drugs significantly increased symptomatic improvement and significantly reduced recurrence rates compared with antimicrobial drugs alone (recurrence rates assessed by culture of expressed prostatic secretion; P = 0.02; no RR or CI reported; 5 people withdrew from treatment).

Harms:

Alpha-blockers versus placebo:
We found no RCTs.

Alpha-blockers plus antimicrobial drugs versus antimicrobial drugs alone:
The RCT comparing alpha-blockers plus antimicrobial drugs versus antimicrobial drugs alone reported no adverse effects of alpha-blockers. [31]

A drug safety alert has been issued on risk of intraoperative floppy iris syndrome during cataract surgery with tamsulosin (http://www.mhra.gov.uk/home/groups/is-insp/documents/websiteresources/con2031031.pdf).

Comment:

Clinical guide:
Some physicians think that treatment of chronic bacterial prostatitis with oral antimicrobial drugs (typically given as a first-line treatment) can be supplemented with alpha-blockers, especially in cases where symptoms persist despite eradication of bacteria from prostatic secretions.

OPTION LOCAL INJECTION OF ANTIMICROBIAL DRUGS

Symptom improvement
Locally injected antimicrobial drugs compared with each other Anal submucosal injection of amikacin may be more effective at 3 months than intramuscular injection of amikacin at improving symptoms (measured by NIH-CPSI score) in men with chronic bacterial prostatitis whose prostatic secretions are sensitive to amikacin (low-quality evidence).

Cure rate
Locally injected antimicrobial drugs compared with each other Anal submucosal injection of amikacin may be more effective at 3 months than intramuscular injection of amikacin at improving cure rate (measured by negative bacterial culture) in men with chronic bacterial prostatitis whose prostatic secretions are sensitive to amikacin (low-quality evidence).

Note
We found no direct evidence about whether locally injected antimicrobial drugs are better than no active treatment or no antimicrobial drugs in men with chronic bacterial prostatitis.

For GRADE evaluation of interventions for chronic prostatitis, see table, p 15 .

Benefits:

Local injection of antimicrobial drugs versus placebo or no antimicrobial drugs:
We found no systematic review or RCTs comparing local injection of antimicrobial drugs versus placebo or no treatment.

Local injection of antimicrobial drugs versus each other:
We found one small RCT (50 men with prostatic secretions sensitive to amikacin), which compared anal submucosal injection of amikacin 400 mg daily for 10 days versus intramuscular amikacin 400 mg daily for 10 days. [32] It found that anal submucosal injection of amikacin significantly improved NIH-CPSI score (9.0 with submucosal injection *v* 22.5 with intramuscular injection; P less than 0.05), and significantly increased bacteriological cure rates (negative bacterial culture: 28/30 [93%] with submucosal injection *v* 7/20 [35%] with intramuscular injection; P less than 0.05) at 3 months compared with intramuscular amikacin.

Harms:

Local injection of antimicrobial drugs versus placebo or no antimicrobial drugs:
We found no RCTs.

Local injection of antimicrobial drugs versus each other:
The RCT comparing anal submucosal versus intramuscular amikacin found no obvious adverse effects, other than the passage of slightly blood-stained faeces in 3/30 (10%) men after the first anal submucosal injection. [32] Infection is a theoretical risk of this invasive procedure.

Comment:

One small cohort study (24 men with refractory chronic bacterial prostatitis) found that eradication of infection was eventually achieved, after an unstated period, in 15 men, with gentamicin 160 mg plus cefazolin 3 g injected directly into the prostate through the perineum. [33]

Clinical guide:
There is limited evidence that local injection of antimicrobial drugs improves bacterial eradication rates compared with oral antimicrobial drugs, and treatments of this type remain experimental.

OPTION NSAIDS FOR CHRONIC BACTERIAL PROSTATITIS

We found no direct information about NSAIDs in the treatment of men with chronic bacterial prostatitis.

For GRADE evaluation of interventions for chronic prostatitis, see table, p 15 .

Benefits: We found no systematic review or RCTs on the effects of NSAIDs in men with chronic bacterial prostatitis.

Harms: We found no RCTs.

Comment: **Clinical guide:**
There is no evidence of benefit for NSAIDs in treating chronic bacterial prostatitis. Their use in combination with antimicrobial drugs has not been evaluated, but RCTs would be feasible.

OPTION RADICAL PROSTATECTOMY

We found no direct information about radical prostatectomy in the treatment of men with chronic bacterial prostatitis.

For GRADE evaluation of interventions for chronic prostatitis, see table, p 15 .

Benefits: We found no systematic review or RCTs on the effects of radical prostatectomy in men with chronic bacterial prostatitis.

Harms: We found no RCTs. Case series have found that radical prostatectomy can cause impotence (9–75% depending on age) [34] and varying degrees of urinary stress incontinence. [35] Other potential harms include those associated with any open surgery.

Comment: We found one report of radical prostatectomy in two young men whose refractory bacterial prostatitis caused relapsing haemolytic crises. [36]

OPTION TURP

We found no direct information about TURP in the treatment of men with chronic bacterial prostatitis.

For GRADE evaluation of interventions for chronic prostatitis, see table, p 15 .

Benefits: We found no systematic review or RCTs on the effects of TURP in men with chronic bacterial prostatitis.

Harms: We found no RCTs in men with chronic bacterial prostatitis. One RCT in men with benign prostatic hypertrophy found no significant difference in the incidence of impotence or urinary incontinence between TURP and watchful waiting. [37]

Comment: One retrospective study reported 40–50% cure rates in 50 men with chronic prostatitis treated with TURP. However, proof of bacterial prostatitis was not obtained in many of the men. [38]

QUESTION What are the effects of treatments for chronic abacterial prostatitis/chronic pelvic pain syndrome?

OPTION ALPHA-BLOCKERS FOR CHRONIC ABACTERIAL PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME

Symptom improvement
Compared with placebo Alpha-blockers may be more effective at improving symptoms (measured by NIH-CPSI scores, International Prostate Symptom Score [IPSS], and pain) at 6 weeks to 1 year in men with chronic abacterial prostatitis/chronic pelvic pain syndrome (CP/CPPS) (very low-quality evidence).

Quality of life
Compared with placebo Terazosin seems to be more effective at 14 weeks at improving quality of life in men with CP/CPPS (moderate quality evidence).

For GRADE evaluation of interventions for chronic prostatitis, see table, p 15 .

Benefits:

Alpha-blockers versus placebo:
We found two systematic reviews, [39] [40] and one additional [41] and one subsequent RCT. [42] The first systematic review (search date 1999, 2 RCTs, 50 men) identified one RCT (20 people) comparing alfuzosin 2.5 mg three times daily versus placebo. [39] It found that alfuzosin significantly improved maximal flow time from baseline compared with placebo (15.4–20.3 mL/second with alfuzosin *v* 13.9–15.6 mL/second with placebo; P = 0.01). [43] It found no significant difference in other outcomes (insufficient information was presented to assess comparative effects on symptom scores). The second RCT identified by the review (30 people) found that an alpha-blocker (phenoxybenzamine 10 mg twice daily) significantly improved pain after prostatic massage at 6 weeks compared with placebo (P less than 0.05). [39] The second systematic review (search date not reported, 6 RCTs, 386 men) compared alpha-blockers versus placebo. [40] The review searched from 1999, as 1999 was the year the National Institutes of Health-Chronic Prostatitis Symptom Index [NIH-CPSI] was first available for use. Meta-analysis of the data was unable to be performed owing to differences in data reporting and outcome interpretation, despite all studies having used the NIH-CPSI to monitor response. Two RCTs were published as abstracts and are therefore not reported here.The review concluded that there was insufficient evidence to fully support alpha-blocker use for CP/CPPS. [40] The first included RCT (70 men) compared three treatments for 6 months with follow-up for a further 6 months: alfuzosin 5 mg twice daily, standard treatment (hot Sitz baths plus anti-inflammatory drugs), and placebo (see comment below). [44] However, only 40 men were randomly allocated to alfuzosin and placebo; 30 men who did not wish to be entered into the randomisation received standard treatment. The RCT found that alfuzosin improved symptoms and reduced pain after 6 months of treatment compared with placebo (change in total NIH-CPSI score from baseline: –9.9 with alfuzosin *v* –3.8 with placebo; change in NIH-CPSI pain score from baseline: –5.1 with alfuzosin *v* –1.1 with placebo; P values not reported). This effect was sustained at 12 months (6 months after treatment finished; change in NIH-CPSI total score from baseline: –3.5 with alfuzosin *v* –0.1 with placebo; P value not reported). [44] The second included RCT (86 men) compared terazosin (with dose escalation from 1–5 mg/day) for 14 weeks versus placebo. [45] It found that terazosin significantly improved quality of life and significantly reduced pain at 14 weeks compared with placebo (NIH-CPSI quality-of-life score 0–2: 24/43 [56%] with terazosin *v* 14/43 [33%] with placebo; P = 0.03; reduction in NIH-CPSI pain score less than 50% from baseline: 26/43 [60%] with terazosin *v* 16/43 [37%] with placebo; P = 0.03). It found no significant difference between terazosin and placebo in peak urinary flow rate (change in peak flow rate: from 15.4 to 18.7 mL/second with terazosin *v* from 18.1 to 19.7 mL/second with placebo) or post-void residual urine (change in residual volume: from 24.8 to 17.1 mL with terazosin *v* from 20.6 to 16.0 mL with placebo; P values not reported). [45] The third included RCT (58 men aged less than 55 years) compared tamsulosin versus placebo. [46] It found that tamsulosin significantly improved symptoms after 45 days compared with placebo (difference in change in NIH-CPSI scores from baseline –3.6, 95% CI –7.0 to –0.3; P = 0.04). Subgroup analyses found that the relative benefit of tamsulosin was greater in men with more-severe symptoms at baseline. The fourth included RCT found no significant difference in improvement in NIH-CPSI scores after 6 weeks of treatment between tamsulosin and no tamsulosin (P less than 0.2). [47] The additional RCT (60 men) compared doxazosin versus placebo. [41] The RCT found that doxazosin significantly improved mean International Prostate Symptom Score (IPSS) compared with placebo at 3 months after cessation of treatment (baseline to 3 months after cessation of treatment, measured on a scale of 0–35: 9.8 to 5.9 with doxazosin *v* 9.3 to 8.8 with placebo; P = 0.001). Subgroup analysis found that men with more-severe symptoms at baseline were significantly more likely to show improved IPSS (P less than 0.001) and pain scores (P less than 0.01) than those with mild symptoms. [41] See benefits of oral antimicrobial drugs, p 12 .

Alpha-blockers versus each other:
We found no systematic review or RCTs.

Harms:

Alpha-blockers versus placebo:
The first RCT identified by the review reported a transient decrease in systolic blood pressure in four people, and a slight decrease in libido in two people treated with alfuzosin. [39] The first RCT in the second systematic review found no withdrawals due to adverse effects with any treatment (alfuzosin, placebo, or standard treatment). [44] It reported that one man (5%) experienced heartburn and four men (21%) experienced decreased ejaculate volume with alfuzosin. The second RCT in the second systematic review found that terazosin significantly increased treatment-related adverse effects compared with placebo (18/43 [42%] with terazosin *v* 9/43 [21%] with placebo; P = 0.04). [45] The most common adverse effects (dizziness [7/43 {16%} with terazosin *v* 2/43 {5%} with placebo] and asthenia [7/43 {16%} with terazosin *v* 3/43 {7%} with placebo; P values not reported]), were more common with terazosin. The third RCT in the second systematic review [46] and the first additional RCT [41] gave no information on adverse effects. The subsequent RCT reported a higher proportion of people with adverse events in the monotherapy group (alpha-blocker alone) and the triple-therapy group (alpha-blocker plus anti-inflammatory plus muscle relaxant) than in the placebo group (12/30 [40%] with alpha-blocker *v* 17/30 [56%] with triple therapy *v* 7/30 [23%]

with placebo; P value not reported). [42] The most common adverse events were dizziness (3/30 [10%] with alpha-blocker *v* 4/30 [13%] with triple therapy *v* 2/30 [7%] with placebo; P value not reported), postural hypotension (3/30 [10%] with alpha-blocker *v* 4/30 [13%] with triple therapy *v* 1/30 [3%] with placebo; P value not reported), and gastrointestinal complaints (2/30 [7%] with alpha-blocker *v* 6/30 [20%] with triple therapy *v* 2/30 [7%] with placebo; P value not reported). [42]

A drug safety alert has been issued on risk of intraoperative floppy iris syndrome during cataract surgery with tamsulosin (http://www.mhra.gov.uk/home/groups/is-insp/documents/websiteresources/con2031031.pdf).

Alpha-blockers versus each other:
We found no RCTs.

Comment:

Alpha-blockers versus placebo:
Two of the RCTs in the second systematic review showed that duration of treatment is important to obtain maximum response. However, before definitive conclusions can be drawn, adequately powered studies with more participants need to be performed. The systematic review reported that alpha-blockers are more likely to be beneficial when treatment duration is longer than 3 months. [40] One quasi-randomised RCT (90 men) compared doxasosin (4 mg/day, monotherapy) versus doxasosin (4 mg/day) plus anti-inflammatory ibuprofen (400 mg/day) plus muscle relaxant therapy (tiocolchicoside 12 mg/day) (triple-therapy) versus placebo. [42] The subjects were randomised in the order they appeared. Both treatment arms (30 patients each) found that the alpha-blocker significantly improved mean NIH-CPSI scores versus placebo (30 patients) after 6 months of treatment (23.1 to 10.7 [decrease of 12.4] with alpha-blocker *v* 21.9 to 9.2 [decrease of 12.7] with combination therapy *v* 22.9 to 21.9 [decrease of 1.0] with placebo; P less than 0.001). The RCT found that combination therapy did not significantly improve mean NIH-CPSI scores compared with alpha-blockers alone (figures not reported, P greater than 0.05). It found that treatment responses were long lasting, with significant improvement in mean NIH-CPSI scores at 12 months in both treatment arms (23.1 to 12.5 [decrease of 10.6] with alpha-blocker *v* 21.9 to 11.7 [decrease of 10.2] for combination therapy *v* 22.9 to 22.2 [decrease of 0.7] for placebo; P greater than 0.001). [42]

Clinical guide:
Most clinicians believe that alpha-blockers are the appropriate first-line treatment for CP/CPPS, despite the lack of strong RCT evidence. However, if alpha-blockers fail to improve symptoms, as determined by the NIH-CPSI, alternative treatments should be investigated.

OPTION 5 ALPHA-REDUCTASE INHIBITORS

Symptom improvement
Compared with placebo We don't know whether 5 alpha-reductase inhibitors are more effective at improving symptoms in men with chronic abacterial prostatitis/chronic pelvic pain syndrome (CP/CPPS) (low-quality evidence).

For GRADE evaluation of interventions for chronic prostatitis, see table, p 15 .

Benefits:

We found one systematic review (search date 1999, 1 RCT, [48] 41 men) [39] and one subsequent RCT, [49] which compared finasteride versus placebo. The RCT included in the review found that, although symptom scores decreased significantly with finasteride after 1 year, there was no significant difference in pain between finasteride and placebo. [48] The RCT was small and had low power (31/41 [75%] of men allocated to finasteride *v* 10/41 [25%] of men allocated to placebo). The subsequent RCT (64 men) found a moderate, but not significant improvement in National Institutes of Health-Chronic Prostatitis Symptom Index (NIH-CPSI) scores in men randomised to 6 months of finasteride compared with placebo (response to treatment defined as more than 25% improvement in NIH-CPSI scores: 33% with finasteride *v* 16% with placebo; P value greater than 0.05). [49]

Harms:

The RCT included in the review reported partial impotence in three men treated with finasteride compared with none in the placebo group. [48] The subsequent RCT found similar rates of adverse effects between treatment and control groups (adverse effects: 5 with finasteride *v* 7 with placebo, significance not reported). [49]

Drug safety alert:
A drug safety alert has been issued on the potential risk of male breast cancer associated with finasteride. (http://www.mhra.gov.uk)

Comment:

Finasteride is known to decrease prostate volume (as it did in the study included in the review; P less than 0.03), but it is unclear how this relates to symptoms of prostatitis. [48]

Clinical guide:
If alpha-blockers fail to provide symptom relief, 5 alpha-reductase inhibitors can be considered as a second-line treatment for men with CP/CPPS.

OPTION ALLOPURINOL

Symptom improvement
Compared with placebo Allopurinol may be more effective at reducing symptoms (measured by an unvalidated "degree of discomfort" score) in men with chronic abacterial prostatitis/chronic pelvic pain syndrome (CP/CPPS) (very low-quality evidence).

For GRADE evaluation of interventions for chronic prostatitis, see table, p 15 .

Benefits: We found one systematic review (search date 2000, 1 RCT, [50] 54 men). [51] The RCT included in the review compared treatment with allopurinol 300 or 600 mg daily versus placebo. [50] Thirty-four men (63%) completed the study, which lasted 240 days. All recorded data were used in the analysis. The RCT found that allopurinol significantly reduced the “degree of discomfort” score (pretreatment score = 0; score –1.1 with allopurinol 300 and 600 mg combined *v* –0.2 with placebo; P = 0.02). [50]

Harms: None of the men receiving allopurinol reported any significant adverse effects, but the RCT did not explain what constituted a significant adverse effect; 55% of people on placebo and 68% of people on allopurinol completed the trial. [50]

Comment: The symptom score was not validated, and the high withdrawal rate makes the results difficult to interpret. [50]

Clinical guide:
If alpha-blockers fail to provide symptom relief, some physicians believe that allopurinol can be considered as a second-line treatment for men with CP/CPPS.

OPTION BIOFEEDBACK

We found no direct information about biofeedback in the treatment of men with chronic abacterial prostatitis/chronic pelvic pain syndrome (CP/CPPS).

For GRADE evaluation of interventions for chronic prostatitis, see table, p 15 .

Benefits: We found no systematic review or RCTs on the effects of biofeedback in men with CP/CPPS.

Harms: We found no RCTs.

Comment: None.

OPTION MEPARTRICIN

Symptom improvement
Compared with placebo We don't know whether oral mepartricin is more effective at improving symptoms in men with chronic abacterial prostatitis/chronic pelvic pain syndrome (CP/CPPS) (low-quality evidence).

Quality of life
Compared with placebo Oral mepartricin may be more effective at improving quality of life (measured by NIH-CPSI) in men with chronic abacterial prostatitis/chronic pelvic pain syndrome (CP/CPPS) (low-quality evidence).

For GRADE evaluation of interventions for chronic prostatitis, see table, p 15 .

Benefits: We found one RCT (26 men) comparing oral mepartricin 40 mg daily with placebo in the treatment of CP/CPPS. [52] It found significant improvements in National Institutes of Health-Chronic Prostatitis Symptom Index (NIH-CPSI) scores for pain and quality of life for mepartricin compared with placebo (median score improvement; pain: –7 with mepartricin *v* –2 with placebo; P = 0.009; quality of life: –5 with mepartricin *v* –1 with placebo; P = 0.0046; total NIH-CPSI score: –15 with mepartricin *v* –5 with placebo; P = 0.0018). The RCT found no significant difference in improvement in NIH-CPSI score for urinary dysfunction for mepartricin compared with placebo (median: –5 with mepartricin *v* –4 with placebo; P = 0.2891). [52]

Harms: One RCT found two cases of mild epigastric pain and nausea. However, no one discontinued treatment because of adverse effects. [52]

Comment: Mepartricin has been shown to form a complex with oestrogen when taken orally, leading to faecal oestrogen excretion and lower plasma oestrogen levels.

Clinical guide:
Mepartricin remains an experimental drug, but some physicians believe that it should be considered as a second-line treatment if alpha-blockers fail to provide symptomatic relief.

OPTION NSAIDS FOR CHRONIC ABACTERIAL PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME

We found no direct information about NSAIDs in the treatment of men with chronic abacterial prostatitis/chronic pelvic pain syndrome (CP/CPPS).

For GRADE evaluation of interventions for chronic prostatitis, see table, p 15 .

Benefits: We found no systematic review or RCTs on the effects of NSAIDs currently used in clinical practice in men with CP/CPPS (see comment below).

Harms: We found no RCTs.

Comment: We found one RCT of sufficient quality comparing rofecoxib (a COX-2 inhibitor) versus placebo in men with CP/CPPS. [53] However, rofecoxib has now been withdrawn from clinical use.

Clinical guide:
The use of NSAIDs for CP/CPPS has been investigated, and early results show moderate efficacy. However, the drugs used in the studies have been withdrawn from clinical use and are not included here.

OPTION PENTOSAN POLYSULFATE

Symptom improvement
Compared with placebo We don't know whether pentosan polysulfate is more effective at improving symptom scores in men with chronic abacterial prostatitis/chronic pelvic pain syndrome (CP/CPPS) (very low-quality evidence).

Quality of life
Compared with placebo Pentosan polysulfate seems more effective at improving quality of life (measured by NIH-CPSI life quality domain score) in men with CP/CPPS (moderate quality evidence).

For GRADE evaluation of interventions for chronic prostatitis, see table, p 15 .

Benefits: We found one systematic review (search date 1999, 1 RCT, [54] 30 men) [39] and one subsequent RCT. [55] The RCT included in the review compared pentosan polysulfate sodium 200 mg twice daily versus placebo. [54] Outcomes included symptom changes by physician rating, symptom score, and uroflowmetry. The RCT found no significant difference in either physician-rated improvement (7/10 [70%] with pentosan polysulfate *v* 5/14 [36%] with placebo; RR 2.00, 95% CI 0.87 to 4.40) or in local symptom scores (proportion of people reporting improvement in symptom score: 5/10 [50%] with pentosan polysulfate *v* 6/14 [43%] with placebo; RR 1.2, 95% CI 0.5 to 2.8) at 3 months. [54] Six people were excluded from the analysis for non-compliance or because they had bacterial prostatitis (analysis was not by intention to treat). The RCT may have been too small to detect important clinical differences between groups. "Physician-rated improvement" is not an objective measurement. There was no significant difference between pentosan polysulfate and placebo in other, more objective and standardised, outcomes. The subsequent RCT (100 men) utilised a larger dose of pentosan polysulfate (300 mg three times daily) and measured outcomes after 16 weeks of treatment. [55] The RCT found a trend toward improved National Institutes of Health-Chronic Prostatitis Symptom Index (NIH-CPSI) scores in all domains with pentosan polysulfate compared with placebo, although only the quality-of-life domain was significant (mean score improvement from baseline; total NIH-CPSI score: 5.9 with pentosan polysulfate *v* 3.2 with placebo; P = 0.081; life quality domain: 2.0 with pentosan polysulfate *v* 1.0 with placebo; P = 0.037; urinary symptoms domain: 1.2 with pentosan polysulfate *v* 0.5 with placebo; P = 0.374; pain domain: 2.7 with pentosan polysulfate *v* 1.7 with placebo; P = 0.21).

Harms: The RCT included in the review found that two men given pentosan polysulfate sodium reported diarrhoea. [54] No men treated with placebo developed gastrointestinal adverse disturbances. The subsequent RCT found a 22% (11/51) withdrawal rate for adverse effects among men randomised to pentosan polysulfate compared with 8% (4/49) for placebo (statistical analysis not reported). [55] The most common adverse effects reported were diarrhoea, nausea, headache, abdominal pain, and back pain. The RCT found no significant difference between groups in the proportion of people

with no adverse effects (P = 1.0) or between groups in the occurrence of individual adverse effects (all P values greater than 0.2). [55]

Comment: **Clinical guide:**
If alpha-blockers fail to provide symptom relief, pentosan polysulfate can be considered as a second-line treatment for men with CP/CPPS.

OPTION QUERCETIN

Symptom improvement
Compared with placebo We don't know whether oral quercetin (a bioflavonoid) is more effective at improving symptoms in men with chronic abacterial prostatitis/chronic pelvic pain syndrome (CP/CPPS) (very low-quality evidence).

For GRADE evaluation of interventions for chronic prostatitis, see table, p 15 .

Benefits: We found one RCT (33 men) comparing oral quercetin 500 mg twice daily for 1 month versus placebo in the treatment of CP/CPPS. [56] It found that National Institutes of Health-Chronic Prostatitis Symptom Index (NIH-CPSI) scores after 1 month of treatment improved significantly in the quercetin group compared with the placebo group (mean improvement in total NIH-CPSI score ± standard deviation: 21 ± 1.8 to 13 ± 1.7 with quercetin *v* 20.2 ± 1.1 to 18.8 ± 1.9 with placebo; P = 0.003). Clinically meaningful improvement (more than 25% improvement in NIH-CPSI scores) was seen in 67% of those taking quercetin compared with 20% taking placebo (P = 0.001). The RCT found no significant improvement in urinary dysfunction with quercetin compared with placebo (P value reported as not significant).

Harms: One RCT reported headaches in one man taking quercetin, and one man noted tingling of extremities. [56] No one stopped treatment because of adverse effects, and all symptoms resolved after cessation of treatment.

Comment: Quercetin is a non-prescription medication. Bioflavonoids have antioxidant properties.

Clinical guide:
Quercetin remains an experimental intervention. However, if alpha-blockers fail to provide symptomatic relief, some physicians think that quercetin can be considered as a second-line treatment for CP/CPPS.

OPTION SITZ BATHS

We found no direct information about sitz baths in the treatment of men with chronic abacterial prostatitis/chronic pelvic pain syndrome (CP/CPPS).

For GRADE evaluation of interventions for chronic prostatitis, see table, p 15 .

Benefits: We found no systematic review or RCTs on the effects of Sitz baths in men with CP/CPPS.

Harms: We found no RCTs.

Comment: None.

OPTION TRANSURETHRAL MICROWAVE THERMOTHERAPY

Symptom improvement
Compared with sham treatment Transurethral microwave thermotherapy may be more effective at 21 months at increasing the proportion of men with an improvement of symptoms (measured by subjective global assessment) in men with chronic abacterial prostatitis/chronic pelvic pain syndrome (CP/CPPS) (very low-quality evidence).

Quality of life
Compared with sham treatment Transurethral microwave thermotherapy may be more effective at 3 months at improving quality of life (measured on a 10-point scale) in men with CP/CPPS (low-quality evidence).

For GRADE evaluation of interventions for chronic prostatitis, see table, p 15 .

Benefits: We found one systematic review (search date 1999, [39] 1 double blind RCT, [57] 20 men). The RCT included in the review compared transurethral microwave thermotherapy versus sham treatment. [57] It found that thermotherapy significantly improved quality of life at 3 months compared with sham treatment (scale 0–10; quality of life improved from 4.4 to 3.0 with transurethral microwave thermotherapy *v* unchanged at 5.2 with sham treatment; P less than 0.05). It found that thermother-

apy significantly increased the proportion of men with improvement of a subjective global assessment by more than 50% over a mean of 21 months compared with sham treatment (7/10 [70%] with transurethral microwave thermotherapy *v* 1/10 [10%] with sham treatment; P value not reported). The review found no good evidence on the effects of thermotherapy on cure or recurrence rate.

Harms: Four men complained of transient (resolved in 3 weeks) adverse reactions, including haematuria (2 men), urinary tract infection, impotence, urinary retention, urinary incontinence, and premature ejaculation (each occurring in 1 man). [57] However, the RCT did not report on whether the men with adverse effects were treated with active treatment or sham treatment.

Comment: Transurethral microwave thermotherapy caused persistent elevation of leucocytes in the prostatic fluid, which could indicate tissue damage.

OPTION ORAL ANTIMICROBIAL DRUGS FOR CHRONIC ABACTERIAL PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME

Symptom improvement

Oral antimicrobial drugs compared with placebo or no ciprofloxacin Oral ciprofloxacin and levofloxacin may be no more effective after 6 weeks at improving symptoms (measured by NIH-CPSI score) in men with chronic abacterial prostatitis/chronic pelvic pain syndrome (CP/CPPS) and a mean symptom duration of 6.2 to 6.5 years (low quality evidence).

For GRADE evaluation of interventions for chronic prostatitis, see table, p 15 .

Benefits: We found two RCTs. [47] [58] The first RCT (196 men, factorial design) compared ciprofloxacin, tamsulosin (an alpha-blocker), combination therapy (ciprofloxacin plus tamsulosin), and placebo for the treatment of CP/CPPS. [47] All treatment groups showed moderate improvement in National Institutes of Health-Chronic Prostatitis Symptom Index (NIH-CPSI) scores after 6 weeks of treatment, but none of the improvements reached significance compared with control (longitudinal regression analysis: ciprofloxacin *v* no ciprofloxacin; P = 0.15; tamsulosin *v* no tamsulosin; P greater than 0.2). The second RCT (80 men) compared levofloxacin (45 men) versus placebo (35 men). [58] It found no significant difference in improvement in NIH-CPSI score between levofloxacin and placebo after 6 weeks of treatment (mean score improvement, measured on scale from 0 to 43: 5.4 with levofloxacin *v* 2.9 with placebo; P = 0.2). However, the treatment group may have been too small to draw reliable conclusions from this study.

Harms: The first RCT found no significant difference in the incidence of adverse effects (mostly gastrointestinal disturbances) between groups. [47] The second RCT reported a 20% (9/45) incidence of mild drug-related effects with levofloxacin, which was not significantly higher than with placebo (20% with levofloxacin *v* 17% with placebo; P value not reported). [58] One person with levofloxacin complained of tendinitis without tendon rupture.

Comment: The men included in the two RCTs had a mean symptom duration of 6.2 [47] and 6.5 [58] years. It is unclear whether the duration of symptoms before treatment affects treatment response, or whether response rates would have been different in treatment-naïve men.

OPTION PROSTATIC MASSAGE

Symptom improvement

Prostatic massage plus antimicrobial drugs compared with antimicrobial drugs alone Prostatic massage plus antimicrobial drugs and antimicrobial drugs alone are equally effective at 4 months at improving symptoms (measured by NIH-CPSI score) in men with chronic abacterial prostatitis/chronic pelvic pain syndrome (CP/CPPS) (moderate-quality evidence).

Note

We found no direct information about whether prostatic massage is better than no active treatment in men with CP/CPPS.

For GRADE evaluation of interventions for chronic prostatitis, see table, p 15 .

Benefits: We found no RCTs comparing prostatic massage with placebo. We found one RCT (81 men) comparing prostatic massage (3 times a week for 4 weeks) in combination with antimicrobial drugs versus antimicrobial drugs alone in men with CP/CPPS. [59] The RCT found no significant differences in final National Institutes of Health-Chronic Prostatitis Symptom Index (NIH-CPSI) scores between the two groups at 4 months' follow-up (mean NIH-CPSI score ± standard deviation: 11.3 ± 8.2 with prostatic massage plus antimicrobial drugs *v* 12.4 ± 7.1 with antimicrobial drugs alone; P greater than 0.05).

Harms: The RCT gave no information on adverse effects of prostatic massage. [59]

Comment: None.

GLOSSARY

Biofeedback Training that helps people to consciously change the vital functions of the body, such as heart rate, which are normally controlled unconsciously.

NIH classification system Category I: *acute bacterial prostatitis* is an acute infection of the prostate. Category II: *chronic bacterial prostatitis* is a recurrent infection of the prostate. Category III: *chronic non-bacterial prostatitis/chronic pelvic pain syndrome (CP/CPPS)*, where there is no demonstrable infection. Subgroups of this class are: (A) inflammatory CPPS (leucocytes seen in semen, prostatic fluid, or urine after prostatic massage); and (B) non-inflammatory CPPS (no leucocytes seen). Category IV: *asymptomatic inflammatory prostatitis*, no subjective symptoms but leucocytes found in prostate/prostatic secretions during work up for other disorders (e.g. on prostate biopsy for prostate cancer). [2]

National Institutes of Health-Chronic Prostatitis Symptom Index (NIH-CPSI) Includes nine items across three domains: pain (4 items; 0–21), urinary symptoms (2 items; 0–10), and quality of life impact (3 items; 0–12). In all domains, higher scores indicate worse outcomes.

Prostatic massage Digital pressure applied to the prostate through the rectum.

Sitz bath A warm water bath taken in the sitting position. The water covers only the hips and buttocks.

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Meares–Stamey The Meares–Stamey test involves collection of four sequential urine samples. Two are taken before prostatic massage; the first from the initial 10 ml and the second from the mid-stream urine. After prostatic massage, the expressed prostatic secretions are collected, as is the initial 10 ml of urine passed after massage. When bacteria and/or inflammatory cells are significantly higher in the two samples after prostatic massage, the pathology is considered to be specific to the prostate.

Moderate-quality evidence Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Very low-quality evidence Any estimate of effect is very uncertain.

SUBSTANTIVE CHANGES

Alpha blockers for chronic abacterial prostatitis/chronic pelvic pain syndrome One systematic review and one RCT added which enhanced the existing benefits and harms data; [40] [42] categorisation unchanged (Likely to be beneficial).

Oral antimicrobial drugs for chronic bacterial prostatitis: One new RCT added, benefits and harms data enhanced. [25] Categorisation unchanged (Likely to be beneficial).

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Bradley A Erickson
Department of Urology
Northwestern University, Feinberg School of Medicine
Chicago
USA

Anthony J Schaeffer
Department of Urology
Northwestern University, Feinberg School of Medicine
Chicago
USA

Brian Van Le
Deptartment of Urology
Northwestern University Medical Centre
Chicago
USA

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Disclaimer

TABLE **GRADE evaluation of interventions for chronic prostatitis**

Important outcomes	Symptom improvement, cure rates, recurrence rates, quality of life, adverse effects								
Number of studies (participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consistency**	**Directness**	**Effect size**	**GRADE**	**Comment**
What are the effects of treatments for chronic bacterial prostatitis?									
2 (443) [23] [24]	Symptom improvement	Oral antimicrobial drugs *v* each other	4	0	0	–1	0	Moderate	Directness point deducted for narrow range of comparators
3 (532) [23] [24] [25]	Cure rates	Oral antimicrobial drugs *v* each other	4	0	0	–1	0	Moderate	Directness point deducted for narrow range of comparators
1 (64) [31]	Recurrence rates	Alpha-blockers plus antimicrobial drugs *v* antimicrobial drugs alone	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
1 (50) [32]	Symptom improvement	Locally injected antimicrobial drugs *v* each other	4	–1	0	–1	0	Low	Quality point deducted for sparse data. Directness point deducted for restricted population
1 (50) [32]	Cure rates	Locally injected antimicrobial drugs *v* each other	4	–1	0	–1	0	Low	Quality point deducted for sparse data. Directness point deducted for restricted population
What are the effects of treatments for chronic abacterial prostatitis/chronic pelvic pain syndrome?									
7 (at least 294) [39] [41] [43] [44] [45] [46] [47]	Symptom improvement	Alpha-blockers *v* placebo	4	–2	–1	0	0	Very low	Quality points deducted for incomplete reporting of results and flaws with randomisation. Consistency point deducted for different results for different outcomes
1 (86) [45]	Quality of life	Alpha-blockers *v* placebo	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
2 (105) [48] [49]	Symptom improvement	5 alpha-reductase inhibitors *v* placebo	4	–2	0	0	0	Low	Quality point deducted for sparse data and incomplete reporting of results
1 (54) [50]	Symptom improvement	Allopurinol *v* placebo	4	–3	0	0	0	Very low	Quality points deducted for sparse data, poor follow-up, and incomplete definition of reported outcome
1 (26) [52]	Symptom improvement	Mepartricin v placebo	4	–1	–1	0	0	Low	Quality point deducted for sparse data. Consistency point deducted for different results for different outcomes
1 (26) [52]	Quality of life	Mepartricin *v* placebo	4	–1	–1	0	0	Low	Quality point deducted for sparse data. Consistency point deducted for different results for different outcomes
2 (124) [54] [55]	Symptom improvement	Pentosan polysulfate *v* placebo	4	–3	0	0	0	Very low	Quality points deducted for sparse data, no intention-to-treat analysis, and for subjective assessment of outcome
1 (100) [55]	Quality of life	Pentosan polysulfate *v* placebo	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (33) [56]	Symptom improvement	Quercetin *v* placebo	4	–2	–1	0	0	Very low	Quality points deducted for sparse data, and incomplete reporting of results. Consistency point deducted for different results for different outcomes

Important outcomes	Symptom improvement, cure rates, recurrence rates, quality of life, adverse effects								
Number of studies (participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consistency**	**Directness**	**Effect size**	**GRADE**	**Comment**
1 (20) [57]	Symptom improvement	Transurethral microwave thermotherapy *v* sham treatment	4	–3	0	0	0	Very low	Quality points deducted for sparse data, incomplete reporting of results, and for subjective outcome measurement
1 (20) [57]	Quality of life	Transurethral microwave thermotherapy *v* sham treatment	4	–2	0	0	0	Low	Quality point deducted for sparse data, and incomplete reporting of results
2 (276) [47] [58]	Symptom improvement	Oral antimicrobial drugs *v* placebo	4	0	0	–2	0	Low	Directness points deducted for too few comparators and for uncertainty about generalisability of results
1 (81) [59]	Symptom improvement	Prostatic massage plus antimicrobial drugs *v* antimicrobial drugs alone	4	–1	0	0	0	Moderate	Quality point deducted for sparse data

Type of evidence: 4 = RCT; 2 = Observational; 1 = Non-analytical/expert opinion.
Consistency: similarity of results across studies
Directness: generalisability of population or outcomes
Effect size: based on relative risk or odds ratio