Benign prostatic hyperplasia and male lower urinary tract symptoms (LUTS)

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ABSTRACT

INTRODUCTION: Lower urinary tract symptoms related to benign prostatic hyperplasia (BPH) and bladder outlet obstruction may affect up to 30% of men in their early 70s. Symptoms can improve without treatment, but the usual course is a slow progression of symptoms, with acute urinary retention occurring in 1% to 2% of men with BPH per year. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of medical, herbal, and surgical treatments? We searched: Medline, Embase, The Cochrane Library, and other important databases up to July 2009 (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 63 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, alpha-blockers, beta-sitosterol plant extract, Pygeum africanum, rye grass pollen extract, saw palmetto plant extracts, transurethral electrovaporisation, transurethral Holmium laser enucleation of the prostate, transurethral microwave thermotherapy, transurethral needle ablation, and transurethral resection (including transurethral resection versus transurethral incision, and transurethral resection versus visual laser ablation/laser vaporisation).

QUESTIONS

INTERVENTIONS

MEDICAL TREATMENTS

Beneficial

HERBAL TREATMENTS

Likely to be beneficial

Unknown effectiveness

Unlikely to be beneficial

SURGICAL TREATMENTS

Beneficial

Likely to be beneficial

Unknown effectiveness

To be covered in future updates

Open prostatectomy

Other alternative/complementary treatments

Combination medical therapy

Key points

- Symptomatic benign prostatic hyperplasia (BPH) may affect up to 30% of men in their early 70s, causing urinary symptoms of bladder outlet obstruction.

  Symptoms can improve without treatment, but the usual course is a slow progression of symptoms, with acute urinary retention occurring in 1% to 2% of men with BPH a year.

- Alpha-blockers improve symptoms compared with placebo and more rapidly than with finasteride, and may be most effective in men with more severe symptoms of BPH or with hypertension.

  CAUTION: A drug safety alert has been issued on risk of intraoperative floppy iris syndrome during cataract surgery with tamsulosin and probably other alpha-blockers. People taking an alpha-blocker should inform their eye surgeon.

- 5 Alpha-reductase inhibitors (finasteride and dutasteride) improve symptoms (especially with longer duration of treatment) and reduce the risk of complications of BPH occurring compared with placebo, and are more effective in men with larger prostates.

  CAUTION: A drug safety alert has been issued on the risk of male breast cancer with finasteride. Changes in breast tissue such as lumps, pain, or nipple discharge should be promptly reported for further assessment.
- Saw palmetto plant extracts may be no more effective than placebo at improving symptoms. However, evidence was weak and further good-quality long-term RCTs are needed.
- Beta-sitosterol plant extract may improve symptoms of BPH compared with placebo in the short term.
- We don't know whether rye grass pollen extract or *Pygeum africanum* are also beneficial, as few studies were found.
- Transurethral resection of the prostate (TURP) improves symptoms of BPH more than watchful waiting, and has been shown not to increase the risk of erectile dysfunction or incontinence.

  Some less invasive surgical techniques such as transurethral incision, laser ablation, transurethral Holmium laser enucleation (HoLEP), and transurethral electrovaporisation seem to be as effective as TURP at improving symptoms.

  TURP may be more effective at improving symptoms and preventing re-treatment compared with transurethral microwave thermotherapy, but causes more complications.

  Transurethral microwave thermotherapy reduces symptoms compared with sham treatment or with alpha-blockers, but long-term effects are unknown.

  We don't know whether transurethral needle ablation is effective.

DEFINITION

Benign prostatic hyperplasia (BPH) is defined histologically. Several terms such as "prostatism", "symptoms of BPH", and "clinical BPH" have previously been used to describe male lower urinary tract symptoms (LUTS). These descriptions incorrectly imply that urinary symptoms in the male arise from the prostate. The acronym "LUTS" was introduced in order to avoid this. Increasingly, scientific communications on this syndrome use the term LUTS and avoid the use of the global term BPH. Nevertheless, BPH remains familiar to and commonly used by general practitioners, other clinicians, and patients when searching for clinical information and guidance. Clinically, the syndrome is characterised by lower urinary tract symptoms (urinary frequency, urgency, a weak and intermittent stream, needing to strain, a sense of incomplete emptying, and nocturia) and can lead to complications, including acute urinary retention.

INCIDENCE/ PREVALENCE

Estimates of the prevalence of symptomatic BPH range from 10% to 30% for men in their early 70s, depending on how BPH is defined. [1]

AETIOLOGY/ RISK FACTORS

The mechanisms by which BPH causes symptoms and complications are unclear, although bladder outlet obstruction is an important factor. [2] The best documented risk factors are increasing age and normal testicular function. [3]

PROGNOSIS

Community- and practice-based studies suggest that men with LUTS can expect slow progression of symptoms. [4] [5] However, symptoms can wax and wane without treatment. In men with LUTS secondary to BPH, rates of acute urinary retention range from 1% to 2% a year. [5] [6] [7]

AIMS OF INTERVENTION

To reduce or alleviate LUTS due to BPH; to prevent complications; and to minimise adverse effects of treatment.

OUTCOMES

Symptom improvement: burden of LUTS, including peak urinary flow rate; residual urine volume; rates of acute urinary retention and prostatectomy; self-rated improvement; and adverse effects of treatment. Symptoms are generally measured using the validated International Prostate Symptom Score (IPSS), which includes 7 questions measuring symptoms on an overall scale from 0 to 35, with higher scores representing more frequent symptoms. [8] Older RCTs reported in this review used a variety of symptom-based assessment instruments, including the Boyarsky Symptom Score and the American Urological Association Symptom Index (AUA-SI). **Adverse effects:** any, arising from medical or surgical treatment (symptoms such as dizziness, headache, and vascular-related), ejaculation disorders, sexual dysfunction, requirement for blood transfusion, urinary retention, haematuria, strictures, etc.).

METHODS

Clinical Evidence search and appraisal July 2009. The following databases were used to identify studies for this systematic review: Medline 1966 to July 2009, Embase 1980 to July 2009, and The Cochrane Database of Systematic Reviews 2009, Issue 3 (1966 to date of issue). An additional search was carried out of the NHS Centre for Reviews and Dissemination (CRD) — for Database

of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA). 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 contributor for additional assessment, using predetermined criteria to identify relevant studies. Study design criteria for inclusion in this review were: published systematic reviews of RCTs and RCTs in any language, at least single blinded, and containing >20 individuals of whom >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. We included systematic reviews of RCTs and RCTs where harms of an included intervention were studied applying the same study design criteria for inclusion as we did for benefits. In addition we use a regular surveillance protocol to capture harms alerts from organisations such as the FDA and the MHRA, which are added to the reviews as required. In this review, we compared each intervention versus placebo (in the case of medical or herbal treatments) or sham therapy or waiting list control (in the case of surgery), and compared each intervention versus each other, and reported any studies that we found. To aid readability of the numerical data in our reviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 38). The categorisation of the quality of the evidence (into high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the *Clinical Evidence* population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).

QUESTION What are the effects of medical treatments in men with benign prostatic hyperplasia?

OPTION ALPHA-BLOCKERS

Symptom improvement

Alpha-blockers as a group compared with placebo Alpha-blockers (alfuzosin, tamsulosin, doxazosin, terazosin included in the analysis) seem more effective than placebo at improving symptom scores (measured by International Prostate Symptom Score [IPSS]/American Urological Association Symptom Index [AUA-SI]) and peak flow rates (moderate-quality evidence).

Tamsulosin compared with placebo Tamsulosin seems more effective than placebo at improving symptom scores (measured by IPSS/AUA-SI or Boyarsky Symptom Score) and peak flow rates (moderate-quality evidence).

Terazosin compared with placebo Terazosin may be more effective than placebo at improving symptom scores (measured by IPSS/AUA-SI), reducing nocturia, and increasing peak flow rates, but we don't know whether it is more effective at improving symptom scores measured by the Boyarsky Symptom Score (low-quality evidence).

Alfuzosin compared with placebo Alfuzosin seems more effective than placebo at improving symptom scores (measured by IPSS), peak flow rates, and at increasing the proportion of men who are able to pass urine after catheter removal. It may be no more effective than placebo at preventing urinary retention or in reducing the proportion of men who require surgery at 6 months (moderate-quality evidence).

Doxazosin compared with placebo Doxazosin seems more effective than placebo at improving symptom scores (measured by IPSS/AUA-SI) and peak flow rates (moderate-quality evidence).

Silodosin compared with placebo Silodosin may be more effective than placebo at improving symptom scores (measured by IPSS) at 3 months, but we don't know whether it is more effective at improving peak flow rates (low-quality evidence).

Tamsulosin compared with other alpha-blockers We don't know whether tamsulosin is consistently more effective than all other alpha-blockers (low-quality evidence).

Terazosin compared with other alpha-blockers We don't know whether terazosin is consistently more effective than all other alpha-blockers (low-quality evidence).

Alfuzosin compared with other alpha-blockers We don't know whether alfuzosin is consistently more effective than all other alpha-blockers (low-quality evidence).

Doxazosin compared with other alpha-blockers We don't know whether doxazosin is consistently more effective than all other alpha-blockers (low-quality evidence).

Prazosin compared with other alpha-blockers We don't know whether prazosin is consistently more effective than all other alpha-blockers (low-quality evidence).

Terazosin compared with 5 alpha-reductase inhibitors Terazosin may be more effective than finasteride at improving AUA-SI scores over 1 year. However, evidence was weak (very low-quality evidence).

Alfuzosin compared with 5 alpha-reductase inhibitors Alfuzosin seems more effective than finasteride at improving IPSS scores (moderate-quality evidence).

Doxazosin compared with 5 alpha-reductase inhibitors Doxazosin seems more effective than finasteride at improving IPSS/AUA-SI symptom scores and peak urinary flow rates (moderate-quality evidence).

Tamsulosin compared with 5 alpha-reductase inhibitors Tamsulosin seems more effective than finasteride at improving symptoms (measured by IPSS) at 4 weeks but not at 24 weeks, and seems more effective at improving urinary flow rates at 4 and 12 weeks but not at 24 weeks. Tamsulosin seems less effective than dutasteride at improving symptoms (measured by IPSS) or peak flow at 2 years in men with large prostates (volume 30 cc or greater) and moderate to severe symptoms (IPSS 12 points or greater) (moderate-quality evidence).

Alpha-blockers compared with transurethral microwave thermotherapy Terazosin may be less effective than transurethral microwave thermotherapy at improving symptom scores (measured by IPSS) and peak flow rate (Qmax) at 6 to 12 months, and at reducing re-treatment rates at 18 months (low-quality evidence).

Alpha-blockers compared with saw palmetto plant extracts We don't know whether tamsulosin is more effective than Serenoa repens at improving symptoms (measured by IPSS) or peak flow rates (low-quality evidence).

Note
Alpha-blockers as a group may be associated with an increase in adverse effects such as dizziness, hypotension, or syncope, compared with placebo. However, adverse effects vary by individual alpha-blocker.

For GRADE evaluation of interventions for benign prostatic hyperplasia, see table, p 38 .

Benefits:

Alpha-blockers as a group versus placebo:
We found one systematic review (search date 2006), which examined 4 alpha-blockers commercially available by prescription for symptomatic treatment of benign prostatic hyperplasia (BPH; terazosin, doxazosin, tamsulosin, alfuzosin) and pooled data. [9] It included double-blind RCTs published in English. Trials that were performed with immediate-release alfuzosin were excluded and trials were restricted to those that use the current controlled-release formulation. The review's primary outcome measure was the occurrence of vascular-related events. However, it also reported on efficacy outcomes and included RCTs that reported change from baseline in maximum urinary flow rate (Qmax) or improvement in symptoms (measured by American Urological Association Symptom Index [AUA-SI] or International Prostate Symptom Score [IPSS]). It included 26 RCTs (4 RCTs alfuzosin, 8 RCTs tamsulosin, 7 RCTs terazosin, 2 RCTs doxazosin gastrointestinal therapeutic system [GITS] and 8 RCTs doxazosin; some RCTs included >2 arms) whose treatment duration most commonly ranged from 4 to 24 weeks, although some trials were of longer duration (some 1 or 2 years, maximum 4.5 years). The review found that alpha-blockers significantly improved urinary flow rate and symptoms compared with placebo (see table 1, p 24). [9] The review did not report absolute numbers or identify individual RCTs included in each analysis.

Tamsulosin versus placebo:
We found two systematic reviews (search date 2000, 6 RCTs, 2758 men; [10] search date 2006 [see any alpha-blocker versus placebo above] [9]) and one additional RCT (see table 1, p 24). [11] The reviews found that tamsulosin significantly improved symptom scores and peak urine flow compared with placebo. [10] [9] The additional RCT found that in men catheterised for acute urinary retention, tamsulosin significantly increased the proportion of men not requiring recatheterisation following trial removal of the catheter. [11]

Terazosin versus placebo:
We found two systematic reviews (search date 2001, 10 RCTs, 3941 men; [12] search date 2006 [see any alpha-blocker versus placebo above] [9]) (see table 1, p 24). The first review found that terazosin improved symptoms and peak urinary flow rates compared with placebo. [12] The largest RCT (2084 men) identified by the review found that terazosin significantly improved IPSS compared with placebo. [13] Secondary analysis of one of the RCTs [14] included in the review (1229 men randomised, 1078 men analysed) found that terazosin significantly reduced nocturia compared with placebo after 1 year of treatment. [15] The second review also found that terazosin significantly improved symptoms and peak urinary flow compared with placebo. [9]

Alfuzosin versus placebo:
We found two systematic reviews (search date 2005, 8 RCTs; [16] search date 2006 [see any alpha-blocker versus placebo above] [9]), two additional RCTs, [17] [18] and one subsequent RCT [19] (see table 1, p 24). The reviews found that alfuzosin significantly improved symptoms and peak urinary flow rates compared with placebo. The first review noted that a limitation of the evidence was the short-term follow-up (only 1 RCT >12 weeks). [16] One large RCT (1522 men) [20] included in one review [9] found that alfuzosin significantly improved symptom scores compared with placebo. This RCT found that, compared with placebo, alfuzosin significantly reduced overall "clinical progression" (measured by a composite outcome of occurrence of acute urinary retention and/or surgery and/or IPSS score worsening by 4 points or more), but did not reduce the risk of urinary retention. [20] The two additional RCTs in men catheterised for acute urinary retention due to benign prostatic hypertrophy found that alfuzosin significantly increased the proportion of men who were able to pass urine after catheter removal compared with placebo. [17] [18] One of these RCTs [18] randomised men who successfully passed urine to alfuzosin or placebo for 6 months. [21] It found that alfuzosin significantly decreased the proportion of men requiring surgery compared with placebo at up to 3 months; however, this reduction was not significant at 6 months. The subsequent RCT found significantly improved sexual function (measured by erectile dysfunction) compared with placebo, without adverse effects on ejaculation. [19]

Doxazosin versus placebo:
We found one systematic review (search date 2006; see any alpha-blocker versus placebo above), which found that doxazosin significantly improved symptoms and peak urinary flow rates compared with placebo (see table 1, p 24). [9]

Silodosin versus placebo:
We found one three-armed RCT comparing silodosin, tamsulosin, and placebo (see table 1, p 24). [22] The RCT found that silodosin significantly improved symptom scores compared with placebo, but found no significant difference among groups in urinary flow rates.

Tamsulosin versus other alpha-blockers:
We found two systematic reviews (search dates 2000 [10] and 2001 [12]) (see table 1, p 24). The first review found no significant difference in symptom scores between tamsulosin and alfuzosin or between tamsulosin and prazosin. [10] The second review found no significant difference in symptom scores between tamsulosin and terazosin. [12] We also found 5 subsequent RCTs (see table 1, p 24). [22] [23] [24] [25] [26] One RCT [22] compared tamsulosin versus silodosin and found significantly greater symptom improvement with silodosin, but found no significant difference between groups in improvement in urinary flow, and used a lower 0.2-mg dose of tamsulosin; one RCT [23] compared tamsulosin versus doxazosin and found that doxazosin was significantly more effective at improving symptoms, but found no significant difference between groups in flow rate, whereas another RCT [26] found that both were equally effective at improving symptoms but found quicker onset of improvement and less sexual dysfunction with doxazosin; two RCTs compared tamsulosin versus naftopidil in Japanese men using a lower 0.2-mg dose of tamsulosin and found similar efficacy between groups. [24] [25] One RCT with weak methods was quasi-randomised (allocation was by odd and even birthdates) and it was unclear how many men had initially been randomised (numbers of men excluded for missing data or for taking naftopidil twice a day not reported). [24]

Terazosin versus other alpha-blockers:
We found one systematic review (search date 2001) (see table 1, p 24). [12] The review found no significant difference in symptom scores between terazosin and tamsulosin, and found no difference between terazosin and doxazosin or terazosin and prazosin.

Alfuzosin versus other alpha-blockers:
We found two systematic reviews [10] [12] and two RCTs [27] [28] (see table 1, p 24). The reviews found no significant difference in symptom scores between alfuzosin and tamsulosin or terazosin. [10] The first RCT found no significant difference in symptom scores between alfuzosin and prazosin. [27] The second RCT found that doxazosin significantly improved symptoms compared with alfuzosin, but the mean doses of the medications used were not equipotent. [28]

Doxazosin versus other alpha-blockers:
We found one systematic review [12] and 5 RCTs, [28] [29] [23] [26] two of which (with a total of 1475 men) were combined in a single analysis (see table 1, p 24). [29] The review found no significant difference in symptom scores between doxazosin and terazosin. [12] The first RCT found that doxazosin significantly improved symptoms compared with alfuzosin, but the mean doses of the medications used were not equivalent. [28] The two combined RCTs found no significant difference between standard and controlled-release doxazosin in symptom scores. [29] One RCT [23] compared doxazosin versus tamsulosin and found that doxazosin was significantly more effective at improving symptoms, but found no significant difference between groups in flow rate, whereas another RCT

[26] found that they were equally effective at improving symptoms but found quicker onset of improvement and less sexual dysfunction with doxazosin.

Prazosin versus other alpha-blockers:
We found two systematic reviews, [10] [12] which found no significant difference in symptom scores between prazosin and tamsulosin or terazosin (see table 1, p 24).

Terazosin versus 5 alpha-reductase inhibitors:
We found one systematic review (search date 2001, 1 RCT, [14] 1229 men) (see table 1, p 24). [12] The RCT [14] identified by the review [12] was of poor quality. It found that terazosin significantly reduced the AUA-SI score compared with finasteride at 1 year.

Alfuzosin versus 5 alpha-reductase inhibitors:
We found one RCT (1051 men) (see table 1, p 24). [30] It found that alfuzosin significantly decreased symptoms from baseline compared with finasteride.

Doxazosin versus 5 alpha-reductase inhibitors:
We found two RCTs, both of which compared 4 interventions (see table 1, p 24). [31] [32] The first RCT found that doxazosin significantly improved total IPSS and peak urinary flow rate over 1 year compared with finasteride alone. [31] The second RCT found that doxazosin improved symptoms but not overall clinical progression compared with finasteride. [32]

Tamsulosin versus 5 alpha-reductase inhibitors:
We found two RCTs comparing tamsulosin versus finasteride [33] [34] (see table 1, p 24). The first RCT found that tamsulosin improved symptoms compared with finasteride at 4 weeks but not at 24 weeks. [33] The second RCT found that tamsulosin significantly improved urinary flow compared with finasteride after 12 weeks. [34] We found one RCT [35] and one subsequent subgroup analysis of the RCT [36] comparing tamsulosin, dutasteride, and tamsulosin plus dutasteride. We have only reported the tamsulosin versus dutasteride comparison here (see comment below). The RCT (4844 men in total: 1623 men with dutasteride; 1611 men with tamsulosin) reported 2-year data from a 4-year study of men with moderate to severe symptoms and enlarged prostate [35] and also reported a subgroup analysis from a subset population of men who reported their ethnicity as Asian (325 men). [36] By 24 months, dutasteride significantly improved symptoms compared with tamsulosin in the whole study population, and results were similar in the Asian subgroup population although the subgroup analysis did not directly test differences between groups (see table 1, p 24).

Alpha-blockers versus transurethral microwave thermotherapy:
See benefits of transurethral microwave thermotherapy, p 15 .

Alpha-blockers versus saw palmetto plant extracts:
See benefits of saw palmetto plant extracts, p 10 .

Harms:

Alpha-blockers as a group versus placebo:
The systematic review (search date 2006) found that alpha-blockers as a group and alfuzosin, terazosin, and doxazosin individually were associated with a significantly greater risk of vascular-related events compared with placebo (see table 1, p 24 ; vascular-related events were defined as the occurrence of one of the following: dizziness, hypotension, or syncope). [9] One non-systematic review of RCTs (3 RCTs, 830 men) suggested that both selective and less selective alpha-blockers may be associated with abnormal ejaculation; the risk of abnormal ejaculation was significantly higher with tamsulosin than with placebo (4.5% with tamsulosin *v* 1.0% with placebo; P = 0.042). [37]

Tamsulosin versus placebo:
One systematic review found no significant difference between tamsulosin and placebo in withdrawal because of adverse events (see table 1, p 24). [10] The additional RCT reported that the overall incidence of adverse events was similar with tamsulosin and placebo (no further data reported; significance not reported). Dizziness, somnolence, and withdrawals due to adverse events were more common with tamsulosin than with placebo, but the significance of these differences was not reported (see table 1, p 24). [11]

Terazosin versus placebo:
One systematic review found that terazosin significantly increased adverse events compared with placebo (see table 1, p 24). [12]

Alfuzosin versus placebo:
One review found that dizziness was the most commonly reported adverse effect and that alfuzosin significantly increased dizziness compared with placebo (see table 1, p 24). [16] One additional

RCT found that more people had adverse events with alfuzosin than with placebo, but no statistical comparisons were performed. [17] Another additional RCT found that withdrawal due to adverse events at 6 months was greater with placebo than with alfuzosin (see table 1, p 24). [18]

Doxazosin versus placebo:
The review found an increased risk of vascular-related events with doxazosin compared with placebo (see table 1 , p 24). [9]

Silodosin versus placebo:
The RCT found that silodosin significantly increased drug-related adverse effects compared with placebo (see table 1 , p 24). [22]

Tamsulosin versus other alpha-blockers:
We found two systematic reviews assessing harms (see table 1, p 24). [10] [12] The first review found no significant difference in withdrawal between tamsulosin and alfuzosin or prazosin. [10] It found no significant difference between tamsulosin and alfuzosin in dizziness, asthenia, or headache. The review also found that the risk of abnormal ejaculation increased with increasing dose of tamsulosin. The second review found that tamsulosin reduced discontinuation of treatment due to adverse effects compared with terazosin. [12] One subsequent RCT reported more abnormal ejaculation with silodosin than with tamsulosin (see table 1, p 24). [22]

Terazosin versus other alpha-blockers:
One systematic review found no significant difference in discontinuation rates between terazosin and either prazosin or doxazosin (see table 1, p 24). [12] The review found no significant difference between terazosin and alfuzosin in dizziness. It found no significant difference in dizziness or headache between terazosin and doxazosin but it may have lacked power to exclude a clinically important effect. The review found that terazosin increased discontinuation of treatment due to adverse effects compared with tamsulosin.

Alfuzosin versus other alpha-blockers:
The reviews found no significant difference in adverse effects between alfuzosin and tamsulosin or terazosin. [10] [12] One RCT found that doxazosin increased withdrawals due to adverse events compared with alfuzosin, but found that similar proportions of men reported any adverse event, dizziness, and serious adverse events with alfuzosin and doxazosin (see table 1, p 24). [28]

Doxazosin versus other alpha-blockers:
The review found no significant difference between terazosin and doxazosin in adverse events. [12] One RCT found that doxazosin increased withdrawals due to adverse events compared with alfuzosin, but found that similar proportions of men reported any adverse event, dizziness, and serious adverse events with alfuzosin and doxazosin. [28] The two combined RCTs found a similar rate of adverse events with standard and controlled-release doxazosin. [29]

Prazosin versus other alpha-blockers:
The two systematic reviews [10] [12] found no significant difference in withdrawal between prazosin and tamsulosin or terazosin (see table 1, p 24).

Terazosin versus 5 alpha-reductase inhibitors:
One RCT identified by the systematic review found that terazosin increased adverse events compared with finasteride (see table 1, p 24). [12]

Alfuzosin versus 5 alpha-reductase inhibitors:
The RCT gave no information on adverse effects. [30]

Doxazosin versus 5 alpha-reductase inhibitors:
The first RCT found that doxazosin increased asthenia, dizziness, and hypotension compared with finasteride, but withdrawals due to adverse effects were similar in both groups. [31] The second RCT also found increased asthenia, dizziness, and hypotension with doxazosin, whereas decreased libido and erectile dysfunction were more common with finasteride; however, the RCT did not provide statistical comparisons. [32]

Tamsulosin versus 5 alpha-reductase inhibitors:
One RCT found similar rates of adverse effects between finasteride and tamsulosin. [34] One RCT found that overall adverse effects were also similar for tamsulosin and for dutasteride. [35]

Alpha-blockers versus transurethral microwave thermotherapy:
See harms of transurethral microwave thermotherapy, p 15 .

Alpha-blockers versus saw palmetto plant extracts:
See harms of saw palmetto plant extracts, p 10 .

Drug safety alert:
A drug safety alert has been issued on risk of intraoperative floppy iris syndrome during cataract surgery with tamsulosin and other alpha-blocker drugs (www.mhra.gov.uk). People taking alpha-blocker drugs should inform their eye surgeon so they are prepared if this effect occurs during surgery.

Comment:

One included RCT compared combination treatment with tamsulosin plus dutasteride versus either treatment alone. [35] We have not reported results for the combination therapy group as this review does not currently systematically search for drug combination therapies. However, drug combination therapies will be included at the next update of this review.

Men with severe symptoms of BPH can expect the largest absolute fall in their symptom scores with medical treatment. [13] [38] Prazosin, terazosin, and doxazosin lower blood pressure and may be used to treat both hypertension and BPH. [39]

OPTION 5 ALPHA-REDUCTASE INHIBITORS

Symptom improvement
Compared with placebo Finasteride and dutasteride are more effective at improving symptom scores and peak urinary flow rates (moderate-quality evidence).

Compared with terazosin Finasteride may be less effective than terazosin at improving American Urological Association Symptom Index (AUA-SI) scores over 1 year. However, evidence was weak (very low-quality evidence).

Compared with alfuzosin Finasteride seems less effective than alfuzosin at improving International Prostate Symptom Score (IPSS) scores (moderate-quality evidence).

Compared with doxazosin Finasteride seems less effective than doxazosin at improving IPSS/AUA-SI symptom scores and peak urinary flow rates (moderate-quality evidence).

Compared with tamsulosin Finasteride seems less effective than tamsulosin at improving symptoms (measured by IPSS) at 4 weeks but not at 24 weeks, and seems less effective at improving urinary flow rates at 4 and 12 weeks but not at 24 weeks. Dutasteride seems more effective than tamsulosin at improving symptoms (measured by IPSS) or peak flow at 2 years in men with large prostates (volume 30 cc or greater) and moderate to severe symptoms (IPSS 12 points or greater) (moderate-quality evidence).

Compared with saw palmetto plant extracts We don't know whether finasteride is more effective than Serenoa repens at improving symptoms (measured by IPSS) or peak flow at 26 weeks (low-quality evidence).

For GRADE evaluation of interventions for benign prostatic hyperplasia, see table, p 38 .

Benefits:

5 Alpha-reductase inhibitors versus placebo:
We found one systematic review (search date 2001, 19 RCTs, 14,729 men) [42] and three subsequent RCTs. [31] [32] [43]

The systematic review found that finasteride 5 mg daily improved total symptom score, maximum urinary flow rate, and prostate volume compared with placebo after a maximum of 48 months of follow-up (results pooled and presented graphically; significance not reported). [42] The largest RCT (multiple publications, 3040 men) identified by the review found that after 4 years of treatment, finasteride 5 mg daily significantly reduced symptom scores compared with placebo (difference in symptom score –1.6 points, 95% CI –2.5 points to –0.7 points [range of score 0–34 points]). [7] [44] [45] [46] [47] It also found that finasteride significantly reduced the risk of acute urinary retention and prostatectomy compared with placebo (urinary retention: 6.6% with placebo *v* 2.8% with finasteride; NNT 26, 95% CI 22 to 38; prostatectomy: 8.3% with placebo *v* 4.2% with finasteride; NNT 24, 95% CI 19 to 37). There was a greater effect among men with higher concentrations of prostate specific antigen at baseline (3.3–12.0 ng/mL), reflecting larger prostates (risk of either acute urinary retention or needing prostatectomy: 19.9% with placebo *v* 8.3% with finasteride; NNT 8, 95% CI 7 to 11). [45] The RCT also found that, after 4 years, finasteride produced a larger fall in International Prostate Symptom Score (IPSS) compared with placebo. The fall was greater for men with prostate specific antigen levels >1.3 ng/mL than for men with prostate specific antigen levels 1.3 ng/mL or less. [44]

The first subsequent RCT (1095 men) compared 4 interventions: finasteride, standard doxazosin, doxazosin plus finasteride, and placebo. [31] It found no significant difference between finasteride

and placebo in IPSS or peak urinary flow rate over 1 year (492 men; P value reported as non-significant, CI not reported). [31]

The second subsequent RCT (3047 men) compared finasteride, doxazosin, finasteride plus doxazosin, and placebo. [32] It found that finasteride significantly reduced the risk of clinical progression (defined as acute urinary retention, urinary incontinence, renal insufficiency, current urinary tract infection, and an increase in the American Urological Association Symptom Index (AUA-SI) score of at least 4 points above baseline) compared with placebo (risk reduction: 34%; P <0.002). [32] It also found that finasteride significantly reduced the risks of acute urinary retention and the need for invasive therapy compared with placebo (risk reduction for acute urinary retention: 68%; P = 0.009; risk reduction for invasive therapy: 64%; P <0.001). [32]

The third subsequent RCT (4325 men) compared dutasteride versus placebo. [43] It found that dutasteride significantly improved AUA-SI scores and peak urinary flow rate after 24 months compared with placebo (improvement in AUA-SI score: 4.5 points with dutasteride *v* 2.3 points with placebo; P <0.001; peak urinary flow rate: +2.2 mL/second with dutasteride *v* +0.6 mL/second with placebo; P <0.001). [43]

5 Alpha-reductase inhibitors versus alpha-blockers:
See benefits of alpha-blockers, p 3 .

5 Alpha-reductase inhibitors versus saw palmetto plant extracts:
See benefits of saw palmetto plant extracts, p 10 .

Harms:

5 Alpha-reductase inhibitors versus placebo:
The systematic review found that the incidence of sexual dysfunction, impotence, ejaculatory disorders, and reduced libido was significantly higher in men treated with finasteride compared with placebo (numbers not reported). [42] One RCT identified by the review (3040 men treated for 4 years) reported harms in some detail. [7] [48] It found that during the first year of the study, 15% of men treated with finasteride and 7% of men treated with placebo experienced treatment-related sexual dysfunction (P <0.001). [48] There was no significant difference in decreased libido (2.6% in both treatment groups) or impotence (5.1% in both treatment groups) between finasteride and placebo, but there was a slightly greater rate of ejaculation disorder with finasteride (0.2% with finasteride *v* 0.1% with placebo; significance not tested). [7] During the remainder of the trial, there was no difference in the incidence of new sexual adverse events between the two groups (7% in both treatment groups). [7] [48] Overall, 4% of men treated with finasteride and 2% of those treated with placebo discontinued treatment due to sexual dysfunction. On discontinuing therapy, 50% of the finasteride group and 41% of the placebo group experienced resolution of their adverse symptoms. Sexual dysfunction resolved in 12% of the men who continued treatment with finasteride and in 19% of those treated with placebo. [48] Although finasteride reduced concentrations of prostate-specific antigen by a mean of 50% (individual responses were highly variable), its use for up to 4 years did not change the rate of detection of prostate cancer compared with placebo. [7] [44] [45] [46] [47]

Two of the subsequent RCTs did not address harms. [31] [43]

One subsequent RCT reported that erectile dysfunction, decreased libido, and abnormal ejaculation occurred significantly more frequently in men treated with finasteride compared with those taking placebo (P <0.05 for all 3 outcomes). [32]

5 Alpha-reductase inhibitors versus alpha-blockers:
See harms of alpha-blockers, p 3 .

5 Alpha-reductase inhibitors versus saw palmetto plant extracts:
See harms of saw palmetto plant extracts, p 10 .

Drug safety alert:
A drug safety alert has been issued on the risk of male breast cancer with finasteride (www.mhra.gov.uk). A review of European clinical trial data, adverse drug reaction reports, and published literature has concluded that an increased risk of male breast cancer associated with finasteride use cannot be excluded. Changes in breast tissue such as lumps, pain, or nipple discharge should be promptly reported for further assessment.

Comment:

5 Alpha-reductase inhibitors versus placebo:
We found two non-systematic reviews comparing finasteride versus placebo. [49] [50] One of the non-systematic reviews (6 RCTs) found that finasteride significantly decreased symptom scores compared with placebo (difference in symptom score: –0.9 points, 95% CI –1.2 points to –0.6 points

[range of score 0–30 points]). [50] The benefit over placebo was greatest in men with larger prostates (40 g or more). The other non-systematic review (meta-analysis of 3 RCTs) found that finasteride reduced acute urinary retention requiring catheterisation after 2 years from 2.7% to 1.1%. [49] The meta-analysis also found that finasteride was significantly more effective than placebo in men with larger prostates at 1 to 2 years. However, the absolute difference in mean decrease of symptom score from baseline between men with the smallest and largest prostates was only about 1 point. The relative effectiveness of finasteride compared with placebo also seemed higher in men with slightly raised prostate-specific antigen levels (assumed to be a proxy for a larger prostate). [44]

QUESTION What are the effects of herbal treatments in men with benign prostatic hyperplasia?

OPTION SAW PALMETTO PLANT (SERENOA REPENS) EXTRACTS

Symptom improvement

Compared with placebo Serenoa repens may be no more effective than placebo at improving symptoms (measured by International Prostate Symptom Score [IPSS]) or peak flow rates (low-quality evidence).

Compared with alpha-blockers We don't know whether Serenoa repens is more effective than tamsulosin at improving symptoms (measured by IPSS) or peak flow rates (low-quality evidence).

Compared with 5 alpha-reductase inhibitors We don't know whether Serenoa repens is more effective than finasteride at improving symptoms (measured by IPSS) or peak flow at 26 weeks (low-quality evidence).

For GRADE evaluation of interventions for benign prostatic hyperplasia, see table, p 38 .

Benefits:

Saw palmetto plant extracts versus placebo:

We found one systematic review (search date 2008). [40] The review included RCTs of *Serenoa repens* in men with symptomatic benign prostatic hyperplasia (BPH) with a treatment duration of at least 30 days. Of 30 RCTs in total included in the review (not all of which were versus placebo or reported demographic data), the mean follow-up was 19.1 weeks (range 4–60 weeks), the average age was 65 years (range 43–88 years), the percentage of men lost to follow-up was 11% (range 0–21%), and 4400/4898 (90%) of study participants were European and 498/4898 (10%) were American. The review also included an analysis of *Serenoa repens* plus other agents (including beta-sitosterol, vitamin E, *Urtica dioica*, and soybean oil, among others). We have only reported on *Serenoa repens* alone here. Two RCTs measured symptoms using the validated International Prostate Symptom Score (IPSS) (see comment below). The review found no significant difference between *Serenoa repens* and placebo in symptom scores measured by IPSS (IPSS total score 0–35, with 35 most severe: 2 RCTs, 304 men; WMD –0.77, 95% CI –2.88 to +1.34; P = 0.47). The review found no significant difference between *Serenoa repens* and placebo in peak urine flow at trial endpoint (10 RCTs, 1019 men; mean difference +1.02 mL/second, 95% CI –0.14 mL/second to +2.19 mL/second; P = 0.084). It also found no significant difference between groups in mean change in peak urine flow or in prostate size at endpoint (peak urine flow: 2 RCTs, 304 men; WMD +0.31 mL/second, 95% CI –0.56 mL/second to +1.17 mL/second; P = 0.49; prostate size at endpoint: 2 RCTs, 243 men; mean difference –1.05 cc, 95% CI –8.84 cc to +6.75 cc). The review found that *Serenoa repens* significantly improved nocturia compared with placebo (9 RCTs, 581 men; mean difference –0.78 times/evening, 95% CI –1.34 times/evening to –0.22 times/evening; P = 0.0061). However, there was significant heterogeneity among RCTs (I^2 = 66%; P = 0.003). A sensitivity analysis restricted to higher-quality larger RCTs (>40 men) found no significant difference in nocturia between groups (5 RCTs; mean difference –0.31 nocturnal visits, 95% CI –0.70 nocturnal visits to +0.08 nocturnal visits; P >0.05; absolute numbers not reported) with little evidence of heterogeneity (I^2 = 11%; P value not reported). [40] The review noted that there had been relatively few high-quality long-term studies evaluating standardised preparations at potentially clinically relevant doses, and that further high-quality RCTs using validated outcome measures with a minimum follow-up of 1 year were needed.

Saw palmetto plant extracts versus alpha-blockers:

We found one systematic review (search date 2008), [40] which included one RCT (704 men) [51] of sufficient quality. The RCT included in the review found no significant difference between tamsulosin and *Serenoa repens* in symptoms, peak urine flow, or nocturia (measured by IPSS total score: 542 men; WMD 0, 95% CI –0.89 to +0.89; peak urine flow: 605 men; WMD +0.10 mL/second, 95% CI –0.67 mL/second to +0.87 mL/second; nocturia measured by percentage improvement: 542 men; RR 0.91, 95% CI 0.66 to 1.27; P = 0.59). [40] The review reported that providers were blinded, but allocation sequence generation and allocation concealment were unclear. [40]

Saw palmetto plant extracts versus 5 alpha-reductase inhibitors:
We found one systematic review (search date 2008), which included one RCT (1098 men) comparing *Serenoa repens* versus finasteride. [40] The RCT lasted 26 weeks and 13.4% of men were lost to follow-up. The review found no significant difference between *Serenoa repens* and finasteride in symptoms measured by IPSS total score at trial endpoint (951 men; mean difference +0.40, 95% CI –0.57 to +1.37; P = 0.42). It also found no significant difference between groups in nocturia or in peak urine flow (nocturia: 1 RCT, 1097 men; mean difference –0.05 times/evening, 95% CI –0.49 times/evening to +0.39 times/evening; P = 0.82; Qmax for peak urine flow: 1 RCT, 951 men; WMD –0.5 mL/second, 95% CI –1.91 mL/second to +0.91 mL/second; P = 0.49). The review found that finasteride significantly reduced prostate volume compared with *Serenoa repens* at trial end (951 men; mean difference 4.80 cc, 95% CI 1.42 cc to 8.18 cc; P = 0.0054). [40]

Harms:

Saw palmetto plant extracts versus placebo:
The review found no significant difference between *Serenoa repens* and placebo in any adverse effects (5 RCTs; 49/313 [16%] with *Serenoa repens v* 46/305 [15%] with placebo; RR 1.07, 95% CI 0.76 to 1.51; P = 0.70). [40] It found no significant difference between groups in dizziness, gastrointestinal distress, or headache (all P values <0.05). The most commonly occurring adverse effect was gastrointestinal distress (5% with *Serenoa repens v* 2% with placebo). With regard to study withdrawals, in a comparison of RCTs with a *Serenoa repens* monotherapy arm (15 RCTs; 175/1483 [12%] people) to RCTs with a placebo arm (13 RCTs; 60/721 [8%] people) the review found a significant difference between groups favouring placebo (RR 1.42, 95% CI 1.07 to 1.88; P = 0.01). However, this was an indirect analysis. [40] One RCT included in the review found no significant difference between groups in sexual adverse effects. [52]

Saw palmetto plant extracts versus alpha-blockers:
The RCT [51] included in the review [40] comparing saw palmetto and tamsulosin found that a similar proportion of men withdrew because of adverse events (7.7% with saw palmetto *v* 8.2% with tamsulosin). [51] The risk of ejaculatory disorder was significantly lower with saw palmetto than with tamsulosin (2/349 [1%] with saw palmetto *v* 15/354 [4%] with tamsulosin; P = 0.001). [51]

Saw palmetto plant extracts versus 5 alpha-reductase inhibitors:
The review found a significantly higher proportion of study withdrawals with *Serenoa repens* compared with finasteride (86/553 [16%] with *Serenoa repens v* 61/545 [11%] with finasteride; RR 1.39, 95% CI 1.02 to 1.89; P = 0.035). [40]

Comment:

The RCTs included in the systematic reviews were mainly short term and few used validated symptom scores (only 2 used the IPSS). [40] Different preparations, which may not be equivalent, are available directly to consumers without prescription in many countries. [40] The RCT comparing saw palmetto versus tamsulosin used a standardised preparation of saw palmetto. [51]

OPTION BETA-SITOSTEROL PLANT EXTRACT

Symptom improvement
Compared with placebo Beta-sitosterol plant extracts may be more effective at improving IPPS scores at 4 to 26 weeks (very low-quality evidence).

For GRADE evaluation of interventions for benign prostatic hyperplasia, see table, p 38 .

Benefits:

Beta-sitosterol plant extract versus placebo:
We found one systematic review (search date 1998, 4 RCTs, 519 men), which compared beta-sitosterol versus placebo. [53] The review found that beta-sitosterol significantly reduced the International Prostate Symptom Score at 4 to 26 weeks (2 RCTs; WMD –4.9 points, 95% CI –6.3 points to –3.5 points).

Harms:

Beta-sitosterol plant extract versus placebo:
Gastrointestinal adverse effects were more common with beta-sitosterol than with placebo (1.6% with beta-sitosterol *v* 0% with placebo; CI not reported). [53] Impotence was also more common with beta-sitosterol (0.5% with beta-sitosterol *v* 0% with placebo; CI not reported). Withdrawal rates were similar in both groups (7.8% with beta-sitosterol *v* 8.0% with placebo; CI not reported).

Comment:

The RCTs included in the review were limited by a short follow-up period (maximum 26 weeks). [53] Different preparations are available, which may be of variable content, making it difficult to generalise results.

OPTION RYE GRASS POLLEN EXTRACT

Symptom improvement
Compared with placebo Rye grass pollen extract may be more effective at increasing self-rated improvement and at reducing nocturia at 12 to 24 weeks (very low-quality evidence).

For GRADE evaluation of interventions for benign prostatic hyperplasia, see table, p 38 .

Benefits:

Rye grass pollen extract versus placebo:
We found one systematic review (search date 1997, 2 RCTs, 163 men), which compared rye grass pollen extract versus placebo. [54] It found that pollen extract significantly increased self-rated improvement and significantly reduced nocturia compared with placebo (proportion improved: 1 RCT, 60 men; 20/31 [65%] with pollen *v* 7/26 [27%] with placebo; RR 2.40, 95% CI 1.21 to 4.75; NNT 3, 95% CI 2 to 9; proportion with reduced nocturia: 2 RCTs; 50/79 [63%] with pollen *v* 23/74 [31%] with placebo; RR 2.05, 95% CI 1.41 to 3.99). However, the results should be interpreted with caution (see comment below).

Harms:

Rye grass pollen extract versus placebo:
The review found that nausea occurred in one man taking pollen extract (number in placebo group not reported). [54] Withdrawal rates were not significantly different (4.8% with pollen *v* 2.7% with placebo; P = 0.26).

Comment:

Both RCTs included in the review were limited by small sample sizes and a short follow-up period (12 and 24 weeks). [54] Concealment of treatment allocation was unclear. The composition of the preparations was unknown, making it difficult to generalise results.

OPTION PYGEUM AFRICANUM

Symptom improvement
Compared with placebo Pygeum africanum may be more effective at increasing peak urinary flow and at reducing residual urine volume at 4 to 16 weeks (very low-quality evidence).

For GRADE evaluation of interventions for benign prostatic hyperplasia, see table, p 38 .

Benefits:

***Pygeum africanum* versus placebo:**
We found one systematic review (search date 2000, 18 RCTs, 1562 men) comparing *P africanum* versus placebo. [55] It found that *P africanum* significantly improved symptoms compared with placebo (5 RCTs, 430 men; proportion with improved symptoms: 65% with *P africanum v* 30% with placebo; RR 2.1, 95% CI 1.4 to 3.1). It also found that *P africanum* significantly increased peak flow compared with placebo at 4 to 16 weeks (4 RCTs, 384 men; mean increase: 23% with *P africanum* compared with placebo; WMD 2.5 mL/second, 95% CI 0.3 mL/second to 4.7 mL/second) and reduced residual urine volume (2 RCTs, 284 men; mean reduction 24% with *P africanum* compared with placebo; WMD –13 mL, 95% CI –23.3 mL to –3.0 mL). [55] These results should be interpreted with caution (see comment below).

Harms:

***Pygeum africanum* versus placebo:**
The RCTs identified by the review gave little information on adverse effects. [55] The review found that adverse events in men taking *P africanum* were "generally mild and similar in frequency to placebo"; the most commonly reported adverse events associated with *P africanum* were gastrointestinal and were reported in 7 men in 5 RCTs (no further data reported).

Comment:

The RCTs included in the review were limited by their short follow-up period (maximum 16 weeks). [55] The designs of the RCTs and the composition of the preparations used varied, making it difficult to generalise results.

QUESTION What are the effects of surgical treatments in men with benign prostatic hyperplasia?

OPTION TRANSURETHRAL RESECTION OF THE PROSTATE

Symptom improvement
Compared with watchful waiting Transurethral resection of the prostate (TURP) is more effective at improving symptom scores at 3 years and at 7.5 months and does not increase the risk of erectile dysfunction or incontinence (high-quality evidence).

Compared with transurethral incision We don't know whether transurethral resection and transurethral incision differ in effectiveness at improving symptom scores (measured by International Prostate Symptom Score [IPSS]) at 1 year or differ in effectiveness at improving peak urine flow at 3 months (low-quality evidence).

Compared with visual laser ablation/laser vaporisation Transurethral resection may be more effective than visual laser ablation/laser vaporisation at improving symptom scores (measured by IPSS/American Urological Association Symptom Index [AUA-SI] scores) and peak flow rates. However, results varied by the timescale examined and the type of analysis undertaken (low-quality evidence).

Compared with contact laser ablation Transurethral resection (TURP) seems more effective than Nd:YAG at improving IPSS symptom scores but not peak urine flow rate. However, when compared with Holmium contact laser, TURP seems more effective at improving peak urine flow rates but not IPSS symptom scores (moderate-quality evidence).

Compared with transurethral Holmium laser resection/enucleation (HoLEP) Transurethral resection (TURP) and HoLEP seem equally effective at improving symptoms (measured by IPSS) at 3 months and 1 year. TURP may be less effective than HoLEP at improving peak urine flow at 3 months and 1 year. However, differences in peak urine flow were small and may not be clinically relevant (moderate-quality evidence).

Compared with transurethral electrovaporisation of the prostate (TUEVP) Transurethral resection and TUEVP seem to be equally effective at improving symptom scores (measured by IPSS/AUA) and peak flow rates at up to 5 years (moderate-quality evidence).

Compared with transurethral electrovaporisation of the prostate (TUEVP) or transurethral Holmium laser resection/enucleation (HoLEP) We don't know whether transurethral resection (TURP), HoLEP, or TUEVP differ in effectiveness at improving symptom scores (measured by IPSS) or peak urine flow (Qmax) at 6 months or 1 year (low-quality evidence).

Compared with transurethral microwave therapy (TUMT) Transurethral resection (TURP) may be more effective than TUMT at improving symptom scores (measured by IPSS or Madsen-Iversen scores) and peak urinary flow (Qmax) at up to 24 months (very low-quality evidence).

Compared with transurethral needle ablation We don't know whether transurethral resection and transurethral needle ablation differ in effectiveness at improving symptoms (measured by IPSS/AUA) at 3 to 18 months, as we found insufficient evidence. Transurethral resection may be more effective than transurethral needle ablation at improving peak urine flow (Qmax) at 3 to 6 months and at reducing re-operations. However, evidence was limited (low-quality evidence).

Note
Recent modification incorporates the use of bipolar current for electrical energy treatments such as transurethral resection and transurethral electrovaporisation, which allows the use of physiological saline as a safer irrigant.

For GRADE evaluation of interventions for benign prostatic hyperplasia, see table, p 38 .

Benefits:

Transurethral resection versus watchful waiting:
We found two RCTs (4 publications) comparing transurethral resection of the prostate (TURP) versus watchful waiting (see table 2, p 36). [56] [57] [58] [59] Both RCTs found that TURP significantly improved symptom scores (at 3 years and 7.5 months) compared with watchful waiting. The first RCT found that TURP reduced treatment failure compared with watchful waiting. [56] [58]

Transurethral resection versus sham treatment:
We found no systematic review or RCTs.

Transurethral resection versus transurethral incision:
We found two systematic reviews (see table 2, p 36). [60] [61] The first review (search date 1999, 9 RCTs) found no significant difference between TURP and transurethral incision in symptom scores. [60] The second review (search date 2006, 11 RCTs [published between 1982 and 2002], 871 men) found no consistent difference between TURP and transurethral incision in symptom scores or flow rate changes; however, evidence was weak and many of the RCTs were small. The review reported that the 11 RCTs were of moderate to poor quality, and that the latest recruitment in the RCTs was in 1990 and so results might not be comparable to current outcomes with TURP given the improvements in TURP technology over the past 16 years. [61]

Transurethral resection versus visual laser ablation/laser vaporisation:
We found two systematic reviews (see table 2, p 36). [62] [61]

The first review (search date 2002, 8 RCTs, 1024 men) found that the results of meta-analysis of symptom scores differed depending on how they were assessed by the RCTs. [62] If mean change

in symptom scores was assessed, TURP reduced symptoms significantly more than visual laser ablation (non-contact laser) at over 6 months' follow-up. However, if mean symptom score at follow-up was assessed, there was no significant difference between TURP and visual laser ablation at 6 or 12 months. The review found that TURP increased peak urine flow compared with visual laser ablation. Longer term follow-up of one of the RCTs (98 men) included in the review found that TURP reduced surgical re-treatment rates after 5 years compared with visual laser ablation. [63]

The second systematic review (search date 2006, 11 RCTs, 854 men) noted that several laser devices could be used to vaporise the prostate, and combined data regardless of the specific method used. [61] The review found that TURP significantly improved symptoms (measured by IPSS/AUA) compared with laser vaporisation at 12 months and 5 years, but found no significant difference between groups at other time points (3 months, 6 months, 2 years). [61] It also found that TURP significantly improved flow rates at 3 and 6 months but not at other time points (1–5 years). [61]

Transurethral resection versus contact laser ablation:
We found one systematic review (search date 2002, 8 RCTs, 851 men [62]) (see table 2, p 36). The review analysed results separately for comparisons of TURP versus Nd:YAG or versus Holmium contact laser. [62] It found that TURP improved symptoms compared with Nd:YAG contact laser, but found no significant difference between treatments in peak urine flow. It found no significant difference between TURP and Holmium contact laser in symptom scores, but found that peak urinary flow was significantly lower with TURP than with Holmium contact laser.

Transurethral resection versus transurethral Holmium laser resection/enucleation (HoLEP):
See benefits of transurethral Holmium laser resection/enucleation (HoLEP), p 18 .

Transurethral resection versus transurethral electrovaporisation of the prostate (TUEVP):
See benefits of transurethral electrovaporisation of the prostate (TUEVP), p 19 .

Transurethral resection versus transurethral microwave therapy (TUMT):
See benefits of transurethral microwave therapy (TUMT), p 15 .

Transurethral resection versus transurethral needle ablation:
See benefits of transurethral needle ablation, p 17 .

Harms:

Analysis of administrative data found that mortality in the 30 days after TURP for benign prostatic hyperplasia ranged from 0.4% for men aged 65 to 69 years to 1.9% for men aged 80 to 84 years, and has fallen in recent years. [64] In one review of observational studies, TURP for benign prostatic hyperplasia was associated with immediate surgical complications in 12% of men, bleeding requiring intervention in 2%, erectile dysfunction in 14%, retrograde ejaculation in 74%, and incontinence in about 5%. [65] [66] [67] Analysis of claims data found a re-operation rate, implying a need for re-treatment, of about 1% a year. [64]

Transurethral resection versus watchful waiting:
The RCTs found that men randomised to prostatectomy did not seem to have a greater rate of erectile dysfunction or incontinence than did men assigned to watchful waiting (see table 2, p 36). [56] [57] [58] [59] The second RCT found that TURP reduced erectile dysfunction and pain or discomfort on ejaculation, but increased ejaculatory dysfunction compared with watchful waiting. [57] [59]

Transurethral resection versus sham treatment:
We found no RCTs.

Transurethral resection versus transurethral incision:
One systematic review found that more men experienced complications, retrograde ejaculation, or required blood transfusion with TURP compared with transurethral prostatic incision; however, the significance of these findings was not reported (see table 2, p 36). [60] The second review found that a significantly greater proportion of men required blood transfusion with TURP compared with transurethral prostatic incision (see table 2, p 36). [61]

Transurethral resection versus visual laser ablation/laser vaporisation:
The first review (search date 2002) found that the RCTs did not comprehensively report adverse effects. [62] Overall, it found that acute urinary retention, urinary tract infections, and dysuria were less common with TURP than with visual laser ablation (see table 2, p 36). The second review found that blood transfusion was significantly more common with TURP compared with visual laser ablation/laser vaporisation, but that retention was significantly less common with TURP (see table 2, p 36). [61]

Transurethral resection versus contact laser ablation:
The review did not report adverse effects separately for Nd:YAG and Holmium contact laser (see table 2, p 36). [62] It found no significant difference in adverse effects between TURP and contact laser ablation.

Transurethral resection versus transurethral Holmium laser resection/enucleation (HoLEP):
See harms of transurethral Holmium laser resection/enucleation (HoLEP), p 18 .

Transurethral resection versus transurethral electrovaporisation of the prostate (TUEVP):
See harms of transurethral electrovaporisation of the prostate (TUEVP), p 19 .

Transurethral resection versus transurethral microwave thermotherapy (TUMT):
See harms of transurethral microwave thermotherapy (TUMT), p 15 .

Transurethral resection versus transurethral needle ablation:
See harms of transurethral needle ablation, p 17 .

Comment: Rapid changes in techniques and too few controlled trials with adequate follow-up make comparisons between TURP and newer surgical techniques difficult. There are also variants of TURP itself that do not fundamentally alter the procedure or outcome in terms of symptomatic improvement or flow but seem to be safer. For example, the use of bipolar current, which enables the use of physiological saline as a safer irrigant. [68] [69]

OPTION TRANSURETHRAL MICROWAVE THERMOTHERAPY (TUMT)

Symptom improvement
Compared with sham treatment Transurethral microwave thermotherapy (TUMT) may be more effective than sham treatment at improving symptoms scores at 3 to 6 months (measured by International Prostate Symptom Score [IPSS] or by Madsen-Iversen scores), be more effective at improving peak flow rates (Qmax) at 3 to 6 months, and be more effective at reducing re-treatment rates (low-quality evidence).

Compared with alpha-blockers Transurethral microwave thermotherapy may be more effective than terazosin at improving symptom scores (measured by International Prostate Symptom Score [IPSS]) and peak flow rate (Qmax) at 6 to 12 months, and at reducing re-treatment rates at 18 months (low-quality evidence).

Compared with transurethral resection (TURP) Transurethral microwave thermotherapy (TUMT) may be less effective than TURP at improving symptom scores (measured by IPSS or Madsen-Iversen scores) and peak urinary flow (Qmax) at up to 24 months (very low-quality evidence).

Note:
We found no RCTs comparing transurethral microwave thermotherapy (TUMT) versus surgical techniques other than transurethral resection. The long-term effects of TUMT have not been adequately evaluated in controlled studies.

For GRADE evaluation of interventions for benign prostatic hyperplasia, see table, p 38 .

Benefits:

Transurethral microwave thermotherapy versus watchful waiting:
We found no systematic review or RCTs.

Transurethral microwave thermotherapy versus sham treatment:
We found two systematic reviews, which reported slightly different analyses but came to similar conclusions. [61] [41]

The first systematic review (search date 2006) included 11 RCTs (1209 men) of generally moderate to poor quality (with respect to conduct and reporting). [61] The review found that transurethral microwave thermotherapy (TUMT) significantly improved symptoms compared with sham surgery at 3 months (International Prostate Symptom Score [IPSS]: 3 RCTs, 298 men; WMD –5.69, 95% CI –7.38 to –3.99; P <0.0001; Madsen-Iversen: 3 RCTs, 238 men; WMD –5.66, 95% CI –6.85 to –4.46). The review reported that the value of longer-term outcomes was limited because of the nature of the comparator (sham treatment) in that by 12 months, most men in the sham group may have required a true procedure, leaving only the least severely affected men in this group, thus introducing selection bias. The review found that TUMT significantly improved flow rate at 3 months compared with sham treatment (Qmax: 5 RCTs, 483 men; WMD 2.53 mL/second, 95% CI 1.69 mL/second to 3.37 mL/second; P <0.00001; significant heterogeneity among RCTs; I^2 = 59.6%; P = 0.03; the heterogeneity not explained by the review). The review found that the percentage of men requiring a re-operation in the TUMT group was significantly less than the percentage of men in the sham group requiring surgery (14/232 [6%] with TUMT *v* 78/145 [54%] with sham; RR 0.14, 95% CI 0.09 to 0.23; P <0.00001; significant heterogeneity among RCTs; I^2 = 75%; P = 0.003).

The heterogeneity was not explained by the review, but it noted that the results should be interpreted with caution as the length of follow-up in RCTs varied. The review noted that data contributing to meta-analysis were too few to provide precise estimates of differences, particularly for complications, and confidence intervals were so wide that clinically important differences could not be ruled out. [61]

The second review (search date 2007) included 7 RCTs (850 men) included in the first review, and excluded the other RCTs included in the first review because of weak methods or for being duplicate or serial reports. [41] The review found that TUMT significantly improved symptoms compared with sham treatment at 3 to 6 months (IPSS: 5 RCTs, 562 men; mean difference –4.75, 95% CI –6.26 to –3.89; significant heterogeneity among RCTs; I^2 = 68%; P = 0.01; Madsen Symptom Score: 2 RCTs, 196 men; mean difference –5.10, 95% CI –6.42 to –3.79; P <0.0001). The review found that TUMT significantly increased flow rate compared with sham treatment at 3 to 6 months (Qmax: 6 RCTs, 643 men; mean difference 1.67 mL/second, 95% CI 0.99 mL/second to 2.34 mL/second; P <0.0001). The review found that re-treatment for benign prostatic hyperplasia (BPH) symptoms occurred significantly less frequently with TUMT compared with sham treatment (1.5/100 person-years with TUMT *v* 13.5/100 person-years with sham treatment; relative hazard 0.12, 95% CI 0.03 to 0.48). [41] The review noted that some studies had important methodological flaws.

Transurethral microwave thermotherapy versus alpha-blockers:
We found one systematic review (search date 2007), which included one RCT (103 men) comparing high-energy TUMT versus terazosin titrated up to a maximal dose of 10 mg daily. [41] The review found that TUMT significantly improved symptoms and peak urinary flow at 6 months compared with terazosin (IPSS: 93 men; mean difference –4.20, 95% CI –5.25 to –3.15; peak flow [Qmax]: 2.30 mL/second, 95% CI 1.47 mL/second to 3.13 mL/second). The review reported that by 18 months symptoms and flow still favoured TUMT (further details including statistical analysis not reported). It found that TUMT significantly reduced re-treatment rates compared with terazosin at 18 months (3/50 [6%] with TUMT *v* 21/43 [49%] with terazosin; RR 0.12, 95% CI 0.04 to 0.38). [41]

Transurethral microwave thermotherapy versus transurethral resection of the prostate:
We found two systematic reviews. [41] [61]

The first review (search date 2007, 6 RCTs) found that transurethral resection of the prostate (TURP) significantly improved symptom scores and peak urinary flow at 6 to 12 months compared with TUMT (IPSS: 5 RCTs, 370 men; mean difference –1.36, 95% CI –2.25 to –0.46; P = 0.0029; peak flow rate [Qmax]: 5 RCTs, 338 men; mean difference 5.08 mL/second, 95% CI 3.88 mL/second to 6.28 mL/second; P <0.0001). [41] It found no significant difference between treatments in quality-of-life scores (measured using IPSS: 1 RCT, 136 men; mean difference –0.67 to +0.47; P = 0.73).

The second review (search date 2006) included 6 RCTs (549 men), of which 4 RCTs were included in the first review. [61] It found that, compared with TUMT, TURP significantly improved symptoms measured by IPSS at 3, 12, and 24 months and measured by Madsen-Iversen scores at 6 months and 12 months (IPSS/AUA: 3 months: 3 RCTs, 290 men; WMD 4.08, 95% CI 2.78 to 5.39; 12 months: 3 RCTs, 286 men; WMD 2.41, 95% CI 1.40 to 3.42; 24 months, 2 RCTs, 113 men; WMD 4.42, 95% CI 2.22 to 6.62; Madsen-Iversen: 6 months: 3 RCTs, 168 men; WMD 1.80, 95% CI 1.05 to 2.54; 12 months: 4 RCTs, 228 men; WMD 1.97, 95% CI 1.27 to 2.44). However, for results measured by IPSS scores at 3 and 12 months, there was significant heterogeneity. The review found that TURP significantly improved flow rates compared with TUMT at 3, 6, 12, and 24 months (3 months: 4 RCTs, 343 men; WMD –5.35, 95% CI –7.09 to –3.62; 6 months: 4 RCTs, 310 men; WMD –4.11, 95% CI –5.21 to –3.01; 12 months: 4 RCTs, 318 men; WMD –5.32, 95% CI –6.95 to –3.70; 24 months, 3 RCTs, 172 men; WMD –6.10, 95% CI –8.21 to –3.99). There was significant heterogeneity in the results for 3, 6, and 12 months. The review reported that the heterogeneity might be caused by differences in disease severity of participants, power delivery, or other technical outputs of surgery across studies. [61]

Harms:

Transurethral microwave thermotherapy versus watchful waiting:
We found no RCTs.

Transurethral microwave thermotherapy versus sham treatment:
The first review found that TUMT significantly increased urinary retention compared with sham treatment (8 RCTs; 77/644 [12%] with TUMT *v* 2/360 [0.5%] with sham; RR 10.57, 95% CI 4.11 to 27.20; P <0.0001). [61] The second review found that, compared with sham treatment, TUMT significantly increased urinary retention, dysuria, and haematuria (urinary retention: 7 RCTs, 812 men; RR 6.04, 95% CI 2.51 to 14.52; self-limited dysuria: 2 RCTs, 298 men; RR 2.40, 95% CI 1.04 to 5.52; haematuria: 2 RCTs, 362 men; RR 3.99, 95% CI 1.28 to 12.46). [41] It found a higher rate of strictures, urinary tract infections, urinary incontinence, and ejaculatory disorders in the TUMT group, although differences between groups were not significant.

Transurethral microwave thermotherapy versus alpha-blockers:
The review found that TUMT significantly reduced the proportion of men with dizziness/asthenia compared with terazosin (0/51 [0%] with TUMT *v* 12/52 [24%] with terazosin; RR 0.04, 95% CI 0 to 0.67). [41] The review found no significant difference between groups in other adverse effects. However, the trial was too small to rule out clinical important differences between treatments in adverse effects.

Transurethral microwave thermotherapy versus transurethral resection of the prostate:
The first systematic review found that TUMT significantly reduced the need for transfusion and reduced retrograde ejaculation, urethral/bladder neck strictures, haematuria, and the transurethral resection syndrome compared with TURP (need for transfusion: 4 RCTs, 249 men [based on 6 events]; RR 0.11, 95% CI 0.01 to 0.86; retrograde ejaculation [sexually active men only]: 78 men; RR 0.39, 95% CI 0.21 to 0.75; strictures: 3 RCTs, 197 men [based on 8 events]; RR 0.13, 95% CI 0.02 to 0.71; requiring surgical treatment for strictures [meatal, urethral, bladder neck]: 5 RCTs; relative hazard 9.76, 95% CI 2.22 to 42.96 [absolute numbers not reported]; haematuria [judged to be serious/requiring additional treatment]: 3 RCTs, 258 men [based on 9 events]; RR 0.25, 95% CI 0.07 to 0.85; transurethral resection syndrome: 3 RCTs, 274 men [based on 6 events]; RR 0.13, 95% CI 0.02 to 0.81). [41] It found that TUMT significantly increased repeat treatment for BPH symptoms, dysuria/urgency, and urinary retention compared with TURP (repeat treatment for BPH symptoms: 4 RCTs; relative hazard 10, 95% CI 2.44 to 50 [absolute numbers not reported]; dysuria/urgency: 3 RCTs, 277 men; RR 2.22, 95% CI 1.28 to 3.86; urinary retention: 4 RCTs, 343 men; RR 2.94, 95% CI 1.52 to 5.70). It found no significant difference between treatments in erectile dysfunction (4 RCTs; 8/140 [6%] with TUMT *v* 10/72 [14%] with TURP; RR 0.41, 95% CI 0.16 to 1.05). [41]

The second review, which included slightly different RCTs from the first review, found no significant difference between groups in blood transfusions, urinary retention, or transurethral resection syndrome. [61] It found that TUMT significantly reduced strictures and length of hospital stay compared with TURP (strictures: 4 RCTs, 340 men; RR 0.20, 95% CI 0.05 to 0.75; length of hospital stay: 1 RCT, 142 men; WMD –5.30 days, 95% CI –6.12 days to –4.48 days). [61]

Comment: TUMT can be performed in an outpatient setting, and uses heat generated by a microwave antenna in the urethra to coagulate prostate tissue. The long-term effects of TUMT have not been adequately evaluated in controlled studies. The systematic reviews comparing TUMT versus TURP reported that all of the included studies had methodological flaws (methods of randomisation and level of blinding not clear and lack of reporting of the change in symptom scores), and in studies following up men for 2 years or more, there were substantial losses to follow-up. [41] [61]

OPTION TRANSURETHRAL NEEDLE ABLATION

Symptom improvement
Compared with transurethral resection (TURP) We don't know whether transurethral needle ablation (TUNA) and TURP differ in effectiveness at improving symptoms (measured by International Prostate Symptom Score [IPSS]/American Urological Association Symptom Index [AUA-SI]) at 3 to 18 months as we found insufficient evidence. TUNA may be less effective than TURP at improving peak urine flow (Qmax) at 3 to 6 months or at reducing re-operations. However, evidence was limited (low-quality evidence).

Note
We found no RCTs comparing TUNA versus watchful waiting or sham treatment, or versus surgical techniques other than transurethral resection.

For GRADE evaluation of interventions for benign prostatic hyperplasia, see table, p 38 .

Benefits:

Transurethral needle ablation versus watchful waiting:
We found no systematic review or RCTs.

Transurethral needle ablation versus sham treatment:
We found no systematic review or RCTs.

Transurethral needle ablation (TUNA) versus transurethral resection (TURP):
We found one systematic review (search date 2006), which found 4 RCTs (450 men). [61] The review found no significant difference between transurethral needle ablation (TUNA) and TURP in symptoms at 3 months, although the result was of borderline significance in favour of TURP (International Prostate Symptom Score [IPSS]/American Urological Association Symptom Index (AUA-SI): 2 RCTs, 165 men [out of 180 randomised]; WMD +1.18, 95% CI –0.03 to +2.40; P = 0.06). One included RCT found that TURP significantly improved symptoms at 12 months (IPSS/AUA: 1 RCT, 100 men [out of 121 randomised]; WMD 3.90, 95% CI 1.27 to 6.53), whereas another found no

significant difference between groups at 18 months (IPSS/AUA: 1 RCT, 57 men [out of 59 randomised]; WMD –0.10, 95% CI –1.52 to +1.32). The review found that TURP significantly improved peak urine flow at 3 and 6 months (3 months: 1 RCT, 59 men [out of 59 randomised]; P <0.00001; 6 months: 1 RCT, 42 men [out of 50 randomised]; P <0.0001). The review found no significant difference between groups in quality of life between 3 months and 5 years; however, these results were largely based on one RCT with poor long-term follow-up. The review found that re-operations were significantly more frequent with TUNA compared with TURP (13/211 [6%] with TUNA *v* 1/212 [0.5%] with TURP; RR 6.89, 95% CI 1.58 to 29.95) and that TUNA significantly increased the duration of operation compared with TURP (1 RCT, 59 men; WMD 11.60 minutes, 95% CI 6.41 minutes to 16.79 minutes; P <0.0001). [61] Overall, the analysis was not by intention to treat, and follow-up was poor in some RCTs. Hence, the results should be interpreted with considerable caution. [61]

Harms:

Transurethral needle ablation versus watchful waiting:
We found no RCTs.

Transurethral needle ablation versus sham treatment:
We found no RCTs.

Transurethral needle ablation (TUNA) versus transurethral resection (TURP):
The review found that, compared with TURP, TUNA significantly reduced blood transfusion, incontinence, stricture, retrograde ejaculation, and erectile dysfunction (blood transfusion: RR 0.05, 95% CI 0.01 to 0.32; incontinence: RR 0.16, 95% CI 0.05 to 0.51; stricture: RR 0.14, 95% CI 0.03 to 0.62; retrograde ejaculation: RR 0.08, 95% CI 0.03 to 0.17; erectile dysfunction: RR 0.11, 95% CI 0.04 to 0.34). [61]

Comment:

TUNA can be performed in an outpatient setting, and uses radiofrequency energy through two intraprostatic electrodes to generate heat to coagulate prostate tissue. Anaesthesia requirements vary in reported studies. We found one further systematic review (search date 2005), including both RCT and observational data, which concluded that TUNA significantly improved benign prostatic hyperplasia parameters with respect to baseline, but did not reach the same level of efficacy as TURP. [71] The long-term effects of treatment have not been adequately evaluated.

OPTION TRANSURETHRAL HOLMIUM LASER RESECTION/ENUCLEATION (HOLEP) New

Symptom improvement
Compared with transurethral resection (TURP) Transurethral Holmium laser resection/enucleation (HoLEP) and TURP seem equally effective at improving symptoms (measured by International Prostate Symptom Score [IPSS]) at 3 months and 1 year. HoLEP may be more effective than TURP at improving peak urine flow at 3 months and 1 year. However, differences in peak urine flow were small and may not be clinically relevant (moderate-quality evidence).

Compared with transurethral electrovaporisation of the prostate (TUEVP) or transurethral resection (TURP) We don't know whether transurethral HoLEP, TUEVP, and TURP differ in effectiveness at improving symptom scores (measured by IPSS) or peak urine flow (Qmax) at 6 months or 1 year (low-quality evidence).

Note
We found no RCTs comparing transurethral HoLEP versus watchful waiting or sham treatment.

For GRADE evaluation of interventions for benign prostatic hyperplasia, see table, p 38 .

Benefits:

Transurethral Holmium laser resection/enucleation (HoLEP) versus watchful waiting:
We found no systematic review or RCTs.

HoLEP versus sham treatment:
We found no systematic review or RCTs.

HoLEP versus transurethral resection (TURP):
We found one systematic review (search date 2006), which compared HoLEP versus TURP and found 5 RCTs (580 men all with severe symptoms and large prostates at trial entry) of moderate quality. [61] The review found no significant difference between groups in symptoms measured by International Prostate Symptom Score [IPSS]/American Urological Association Symptom Index (AUA-SI) at 3 months (2 RCTs, 177 men; WMD –0.47, 95% CI –1.92 to +0.98; P = 0.53). It found that HoLEP significantly improved symptoms measured by IPSS/AUA compared with TURP at 6 months and 1 year (6 months: 5 RCTs, 458 men; WMD –0.91, 95% CI –1.05 to –0.77; P <0.00001; 1 year: 5 RCTs, 311 men; WMD –0.42, 95% CI –0.52 to –0.32; P <0.00001). There was significant heterogeneity among RCTs for the result at 1 year (I^2=74%; P = 0.004). The review performed a random effects analysis for the result at 1 year, and although the WMD still favoured HoLEP, the difference between groups was no longer significant (WMD –0.80, 95% CI –1.70 to +0.10; P = 0.08).

The review found that HoLEP significantly improved peak urine flow rate compared with TURP at 3 months and 12 months (3 months: 2 RCTs, 177 men; WMD 3.49 mL/second, 95% CI 0.63 mL/second to 6.35 mL/second; P = 0.02; 12 months: 5 RCTs, 547 men; WMD 1.43 mL/second, 95% CI 0.92 mL/second to 1.93 mL/second; P <0.00001). The review found that the length of hospital stay was significantly shorter with HoLEP compared with TURP (4 RCTs, 477 men; WMD –1.05 days, 95% CI –1.20 days to –0.89 days). The review found no significant difference between HoLEP and TURP in re-operation rates (4 RCTs; 10/231 [4%] with HoLEP v 15/232 [6%] with TURP; RR 0.68, 95% CI 0.32 to 1.44; P = 0.31). [61] The review noted that although the results for peak urine flow are statistically significant, the difference was small and may therefore not be clinically relevant.

HoLEP versus transurethral electrovaporisation of the prostate (TUEVP) or transurethral resection (TURP):
We found one systematic review (search date 2006), [61] which included one RCT (150 men) comparing HoLEP, TURP, and transurethral vapour resection of the prostate (TUEVP). [70] The RCT reported that all groups had improvement from baseline but found no significant difference among groups in symptom scores (measured by IPSS) at 6 months (P = 0.14) or 1 year (P = 0.6). [70] The RCT found no significant difference among groups in peak urine flow (Qmax) at 6 months (P = 0.33) or 1 year (P = 0.62). The method of randomisation and degree of blinding was not described. [70]

Harms:

Transurethral Holmium laser resection/enucleation (HoLEP) versus watchful waiting:
We found no RCTs.

HoLEP versus sham treatment:
We found no RCTs.

HoLEP versus transurethral resection (TURP):
The review found that HoLEP significantly reduced the proportion of men who required blood transfusion compared with TURP (1/293 [0.3%] with HoLEP *v* 9/287 [3.1%] with TURP; RR 0.27, 95% CI 0.07 to 0.95; P = 0.04). [61] The review found no significant difference between HoLEP and TURP in erectile dysfunction or retrograde ejaculation (erectile dysfunction: 1 RCT, 48 men; RR 1.18, 95% CI 0.18 to 7.71; retrograde ejaculation: 2 RCTs, 91 men; RR 1.14, 95% CI 0.95 to 1.36), although results were based on small numbers.

HoLEP versus transurethral electrovaporisation of the prostate (TUEVP) or transurethral resection (TURP):
The RCT found that blood loss was significantly less with TUEVP or HoLEP than with TURP (68.6 mL with TUEVP *v* 140.5 mL with TURP *v* 40.6 mL with HoLEP; HoLEP or TUEVP *v* TURP; P <0.001). [70] It found no significant difference among groups for changes in haemoglobin (P = 0.22) or serum sodium decrease (P = 0.99). [70]

Comment:

HoLEP requires extra training and expensive equipment and may be restricted to specialist centres, whereas TURP and laser vaporisation are more widely available.

OPTION TRANSURETHRAL ELECTROVAPORISATION OF THE PROSTATE (TUEVP) New

Symptom improvement
Compared with transurethral resection (TURP) Transurethral electrovaporisation of the prostate (TUEVP) and TURP seem equally effective at improving symptom scores (measured by International Prostate Symptom Score [IPSS]/American Urological Association Symptom Index [AUA-SI]) and peak flow rates at up to 5 years (moderate-quality evidence).

Compared with transurethral Holmium laser resection/enucleation (HoLEP) or transurethral resection (TURP) We don't know whether TUEVP, HoLEP, and TURP differ in effectiveness at improving symptom scores (measured by IPSS) or peak urine flow (Qmax) at 6 months or 1 year (low-quality evidence).

Note
We found no RCTs comparing TUEVP versus watchful waiting or sham treatment.

For GRADE evaluation of interventions for benign prostatic hyperplasia, see table, p 38 .

Benefits:

Transurethral electrovaporisation of the prostate versus watchful waiting:
We found no systematic review or RCTs.

Transurethral electrovaporisation of the prostate versus sham treatment:
We found no systematic review or RCTs.

Transurethral electrovaporisation of the prostate (TUEVP) versus transurethral resection of the prostate (TURP):
We found one systematic review (search date 2006), which compared transurethral vaporisation of the prostate using electrosurgical energy (TUEVP) versus transurethral resection of the prostate (TURP). [61] It included 17 RCTs of moderate to low quality. The review found no significant difference between groups in symptom scores measured by International Prostate Symptom Score (IPSS)/American Urological Association Symptom Index (AUA-SI) at 3 months, 1 year, or 5 years (3 months: 7 RCTs, 663 men; WMD +0.09, 95% CI –0.42 to +0.61; P = 0.72; 1 year: 5 RCTs, 438 men; WMD +0.34, 95% CI –0.19 to +0.86; P = 0.21; 5 years: 3 RCTs, 125 men; WMD –0.32, 95% CI –1.95 to +1.31; P = 0.70). The review found no significant difference between groups in peak urine flow (measured by Qmax) at 1 or 5 years (1 year: 5 RCTs, 331 men; WMD –0.11 mL/second, 95% CI –0.97 mL/second to +0.74 mL/second; P = 0.8; 5 years: 3 RCTs, 124 men; WMD +0.60 mL/second, 95% CI –1.06 mL/second to +2.26 mL/second; P = 0.48). The result for 1 year was significantly heterogeneous (I^2 = 73%; P = 0.006). The review reported that some of the variation among RCTs might be explained by differences in participant's characteristics or the ways in which technologies were used. It found no significant difference between groups in re-operation rates (7 RCTs, 672 men; RR 1.04, 95% CI 0.53 to 2.07; P = 0.9). However, confidence intervals were wide. It found no significant difference between groups in duration of operation (8 RCTs, 591 men; WMD –1.62 minutes, 95% CI –12.23 minutes to +8.99 minutes; P = 0.76). For length of stay, 8 RCTs reported data suitable for pooling. The review found that the average length of stay was 1.00 days less following TUEVP than with TURP (8 RCTs, 857 men; WMD –1.00 day, 95% CI –1.25 days to –0.75 days; P <0.00001). [61]

Transurethral electrovaporisation of the prostate (TUEVP) versus transurethral Holmium laser resection/enucleation (HoLEP) or transurethral resection (TURP):
We found one RCT (150 men) comparing TUEVP, HoLEP, and TURP, which found no significant difference among groups in symptoms measured by IPSS or in urinary flow (Qmax) at 6 or 12 months (see benefits of HoLEP, p 18).

Harms:

Transurethral electrovaporisation of the prostate versus watchful waiting:
We found no RCTs.

Transurethral electrovaporisation of the prostate versus sham treatment:
We found no RCTs.

Transurethral electrovaporisation of the prostate (TUEVP) versus transurethral resection of the prostate (TURP):
The review found that TUEVP significantly reduced the proportion of men needing a blood transfusion compared with TURP (13 RCTs; 2/504 [0.4%] with TUEVP *v* 29/537 [5%] with TURP; RR 0.19, 95% CI 0.08 to 0.44; P = 0.0001). [61] It found no significant difference between groups in strictures or bladder neck contractures (11 RCTs, 862 men; RR 0.91, 95% CI 0.45 to 1.85; P = 0.80). It also found no significant difference between groups in the occurrence of transurethral resection syndrome or urinary tract infections (transurethral resection syndrome: 8 RCTs, 643 men; RR 0.59, 95% CI 0.17 to 2.12; P = 0.42; urinary tract infections: 8 RCTs, 616 men; RR 0.65, 95% CI 0.40 to 1.08; P = 0.09). The review found that TUEVP significantly increased the proportion of men with urinary retention compared with TURP (33/389 [8%] with TUEVP *v* 15/419 [4%] with TURP; RR 2.12, 95% CI 1.23 to 3.68; P = 0.007). [61]

Transurethral electrovaporisation of the prostate (TUEVP) versus transurethral Holmium laser resection/enucleation (HoLEP) or transurethral resection (TURP):
See harms of HoLEP, p 18 .

Comment:

Modification of TUEVP itself that does not seem to fundamentally alter the procedure or outcome in terms of symptomatic improvement or flow may improve safety (e.g., the use of bipolar current, which enables the use of physiological saline as a safer irrigant).

GLOSSARY

Transurethral microwave thermotherapy (TUMT) involves the use of a special catheter that contains a microwave antenna. This is passed into the urethra and heats the prostate, which subsequently necroses.

Transurethral needle ablation (TUNA) uses radiofrequency energy, applied through two needle electrodes, which are inserted into the prostate transurethrally. Following the application of radiofrequency energy, the prostate necroses.

Transurethral resection of the prostate (TURP) is performed endoscopically. Cutting diathermy is used to cut away the tissue. Any bleeding is treated by electrocautery and the pieces of prostatic tissue are washed out of the bladder.

American Urological Association Symptom Index (AUA-SI) is a patient questionnaire which asks 7 questions about the severity of symptoms (range 0–35). Mild symptoms score 0–7 points, moderate symptoms 8–19 points, and severe symptoms 20–35 points.

High-quality evidence Further research is very unlikely to change our confidence in the estimate of effect.

Holmium laser resection or enucleation of the prostate (HoLRP or HoLEP) is performed endoscopically. Holmium laser energy through a fibre can be used to cut away strips or chunks of the prostate (HoLRP). More commonly the fibre is used to "enucleate" the prostatic adenoma, leaving the prostatic capsule behind (HoLEP) in a manner very similar to open surgery. Often both techniques are used together.

International Prostate Symptom Score (IPSS) A patient questionnaire that is essentially the same as the American Urological Association Symptom Index (AUA-SI) questionnaire.

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.

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.

Transurethral electrovaporisation of the prostate (TUEVP or simply TUVP) is performed endoscopically. TUEVP is similar to transurethral resection of the prostate (TURP) but uses higher power bipolar or monopolar electrical energy, which is concentrated on an electrode that is applied directly to the prostatic tissue in order to cause tissue vaporisation and removal.

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

SUBSTANTIVE CHANGES

Transurethral Holmium laser resection/enucleation (HoLEP) New option added. [61] [70] Categorised as Likely to be beneficial.

Transurethral electrovaporisation of the prostate (TUEVP) New option added. [61] [70] Categorised as Likely to be beneficial.

5 Alpha-reductase inhibitors New evidence added. [35] [36] [40] Categorisation unchanged (Beneficial).

Alpha-blockers New evidence added. [9] [16] [19] [22] [23] [24] [25] [26] [35] [36] [40] [41] Categorisation unchanged (Beneficial).

Transurethral needle ablation New evidence added. [61] [71] Categorisation unchanged (Unknown effectiveness), as there remains insufficient evidence to judge the effects of this intervention.

Transurethral resection of the prostate Option restructured. Previous two separate options ("transurethral resection of the prostate versus no surgery" and "transurethral resection of the prostate versus other surgical techniques") combined into one option. New evidence added. [41] [61] [68] [70] [69] [71] "Transurethral resection of the prostate" categorised as Beneficial.

Saw palmetto plant (Serenoa repens) extracts Search updated for already included systematic review. [40] New evidence added to the already reported review, which alters its previous conclusions. Categorisation changed from Likely to be beneficial to Unlikely to be beneficial.

Transurethral microwave thermotherapy (TUMT) New evidence added, which suggests that transurethral microwave thermotherapy may be more effective at improving symptoms than sham treatment, but may be less effective at improving symptoms than transurethral resection. [41] [61] Categorisation changed from Beneficial to Likely to be beneficial.

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Disclaimer

TABLE 1 **Alpha-blockers**

Reference study type	Intervention	Population	Benefits	Harms
Alpha-blockers as a group *v* placebo				
Systematic review (search date 2006) [9]	Any alpha-blocker *v* placebo (the review included RCTs on alfuzosin, tamsulosin, doxazosin, terazosin)	26 RCTs	**Peak urinary flow rate (Qmax):** WMD 1.32 mL/minute, 95% CI 1.07 mL/minute to 1.57 mL/minute; P <0.0001 (absolute numbers and RCTs included in analysis not reported) **Symptom score (AUA-SI/IPSS):** WMD –1.92 points, 95% CI –2.71 points to –1.14 points; P <0.0001 (absolute numbers and RCTs included in analysis not reported)	Alpha-blockers were associated with a statistically significant increase in the odds of developing a vascular-related event (dizziness, hypotension, or syncope) compared with placebo (26 RCTs; OR 2.54, 95% CI 2.00 to 3.24; P <0.0001; absolute numbers not reported; statistical heterogeneity among RCTs [P = 0.011]). Results varied by individual agent (see below)
	Subgroup analysis of individual alpha-blockers *v* placebo		**Peak urinary flow rate (Q max):** Alfuzosin: 4 RCTs; WMD 0.84 mL/minute, 95% CI 0.55 mL/minute to 1.13 mL/minute; tamsulosin: 7 RCTs; WMD 1.59 mL/minute, 95% CI 0.92 mL/minute to 2.26 mL/minute; terazosin: 7 RCTs; WMD 1.27 mL/minute, 95% CI 0.91 mL/minute to 1.63 mL/minute; doxazosin: 6 RCTs; WMD 1.73 mL/minute, 95% CI 1.26 mL/minute to 2.21 mL/minute; doxazosin GITS, 2 RCTs; WMD 1.76 mL/minute, 95% CI 1.13 mL/minute to 2.39 mL/minute (all comparisons P <0.0001; absolute numbers not reported) **Symptom score (AUA-SI/IPSS):** Alfuzosin WMD –1.67, 95% CI –2.11 to –1.23; tamsulosin WMD –3.06, 95% CI –4.79 to –1.33; terazosin WMD –3.40, 95% CI –4.29 to –2.51; doxazosin WMD –2.49, 95% CI –3.20 to –1.78; doxazosin GITS WMD –2.16, 95% CI –2.99 to –1.33 (all comparisons P <0.0001; absolute numbers and RCTs included in analysis not reported)	The odds of developing a vascular-related adverse event (dizziness, hypotension, or syncope) relative to placebo were significantly increased with: alfuzosin (4 RCTs; OR 1.66, 95% CI 1.17 to 2.36), terazosin (7 RCTs; OR 3.71, 95% CI 2.48 to 5.53), and doxazosin (doxazosin: 6 RCTs; OR 3.32, 95% CI 2.10 to 5.23; doxazosin GITS: 2 RCTs; OR 3.86, 95% CI 1.86 to 8.02), but not with tamsulosin (7 RCTs; OR 1.42, 95% CI 0.99 to 2.05; P = 0.053) Compared with placebo, alfuzosin significantly increased dizziness (P = 0.04) and dizziness, hypotension, or syncope (P = 0.005); terazosin significantly increased dizziness (P <0.0001), hypotension (P <0.0001), asthenia/fatigue (P <0.0001), and dizziness, hypotension, or syncope (P <0.0001); doxazosin significantly increased dizziness (P <0.0001), hypotension (P <0.0001), asthenia/fatigue (P <0.0001), and dizziness, hypotension, or syncope (P <0.0001); and doxazosin GITS significantly increased dizziness (P = 0.001) and dizziness, hypotension, or syncope (P <0.0001; for ORs of composite outcome of dizziness, hypotension, or syncope, see above)
Tamsulosin *v* placebo				
[10] Systematic review (search date 2000)	**Tamsulosin** (0.4 or 0.8 mg/day) *v* placebo	6 RCTs, 2758 men	**Boyarsky Symptom Score:** WMD for mean change tamsulosin 0.4 mg *v* placebo: –1.1, 95% CI –1.49 to –0.72 WMD for mean change tamsulosin 0.8 mg *v* placebo: –1.6, 95% CI –2.3 to –1.0 **Peak urine flow:** WMD for mean change tamsulosin 0.4 mg *v* placebo: 1.1 mL/second, 95% CI 0.59 mL/second to 1.51 mL/second WMD for mean change tamsulosin 0.8 mg *v* placebo: 1.1 mL/second, 95% CI 0.65 mL/second to 1.48 mL/second	No significant difference in adverse effects between tamsulosin and placebo. Withdrawal because of adverse effects (4 RCTs): RR 1.08, 95% CI 0.72 to 1.62 Abnormal ejaculation (4 RCTs): AR 10.8% with tamsulosin *v* <1% with placebo; RR 17.0, 95% CI 2.5 to 114.0 Rhinitis (4 RCTs): AR 11.2% with tamsulosin *v* 6% with placebo; RR 1.84, 95% CI 1.24 to 2.72 Dizziness (5 RCTs): AR 11.9% with tamsulosin *v* 7.8% with placebo; RR 1.50, 95% CI 1.13 to 1.98

Reference study type	Intervention	Population	Benefits	Harms
[9] Systematic review (search date 2006)	Tamsulosin *v* placebo		See any alpha-blocker *v* placebo above	See any alpha-blocker *v* placebo above
[11] RCT	Tamsulosin (0.4 mg/day for 3 or 8 days, according to study site) *v* placebo	141 men catheterised for acute urinary retention in the previous 72 hours	**Successful trial removal of catheter (no need for re-catheterisation):** AR 34/71 (48%) with tamsulosin *v* 18/70 (26%) with placebo; P = 0.011; OR 2.47, 95% CI 1.23 to 4.97	Similar overall rate of adverse effects for both treatments (no further data reported) Withdrawals due to adverse effects: AR 9% with tamsulosin *v* 1% with placebo Dizziness: AR 10% with tamsulosin *v* 3% with placebo Somnolence: AR 6% with tamsulosin *v* 3% with placebo (significance not reported for any comparison)
Terazosin *v* placebo				
[12] Systematic review (search date 2001)	Terazosin *v* placebo	10 RCTs, 3941 men	**Boyarsky Symptom Score:** Mean improvement in Boyarsky Symptom Score: 4 RCTs; 37% with terazosin *v* 15% with placebo; P value not reported **AUA-SI:** (score range: 0–35, where 0 = no symptoms and 35 = severe symptoms) Mean improvement: 2 RCTs; 38% with terazosin *v* 17% with placebo; P value not reported **Peak urinary flow rate:** Improvement: 23% with terazosin *v* 11% with placebo; P value not reported	Terazosin significantly increased dizziness, asthenia, and postural hypotension compared with placebo Dizziness (6 RCTs): RR 2.43, 95% CI 1.82 to 3.25; Asthenia (5 RCTs): RR 2.24, 95% CI 1.68 to 3.00 Postural hypotension (4 RCTs): RR 5.27, 95% CI 2.59 to 10.72 Discontinuation rates (10 RCTs): 27% with terazosin *v* 34% with placebo; RR 0.94, 95% CI 0.76 to 1.17 Discontinuation because of adverse effects (6 RCTs): 229/1817 (13%) with terazosin *v* 140/1607 [9%] with placebo; RR 1.50, 95% CI 1.23 to 1.83
[13] The largest RCT identified by the review [12]	Terazosin (at doses of up to 10 mg/day for 1 year) *v* placebo	2084 men	**IPSS:** Mean change from baseline: –7.6 points with terazosin *v* –3.7 with placebo; difference in mean change for terazosin *v* placebo: –3.9 points, 95% CI –5.5 points to –3.3 points	Withdrawal due to adverse effects: 19.7% with terazosin *v* 15.2% with placebo; P <0.001
[15] RCT (secondary analysis of an RCT [14] included in review [12])	Terazosin (10 mg/day) *v* placebo *v* finasteride (5 mg/day) *v* terazosin plus finasteride	1229 randomised (1078 men analysed)	**Number of episodes of nocturia:** Mean number after 1 year of treatment: 1.8 with terazosin *v* 2.1 with placebo; P = 0.0001	The RCT gave no information on adverse effects
[9] Systematic review (search date 2006)	Terazosin *v* placebo		See any alpha-blocker *v* placebo above	See any alpha-blocker *v* placebo above
Alfuzosin *v* placebo				

Reference study type	Intervention	Population	Benefits	Harms
[16] Systematic review (search date 2005)	Alfuzosin *v* placebo	8 RCTs (trial size range 30–518 men, treatment duration 4–26 weeks with only 1 trial >12 weeks)	**IPSS score (absolute mean change from baseline):** 3 RCTs, 1373 men; –5.4 points with alfuzosin [dose 7.5–10 mg] *v* –3.6 points with placebo; WMD –1.8 points, 95% CI –2.49 points to –1.11 points (absolute numbers not reported) **Peak urinary flow (change from baseline):** 8 RCTs; 2.6 mL/second (10–54%) with alfuzosin *v* 1.1 mL/second (2–29%) with placebo (statistical analysis between groups not reported) For alfuzosin 10 mg formulation compared with placebo; WMD 1.20 mL/second, 95% CI 0.76 mL/second to 1.64 mL/second (absolute numbers not reported) Alfuzosin compared with placebo at endpoint, 7 RCTs; WMD 0.45 mL/second, 95% CI 0.29 mL/second to 0.60 mL/second (absolute numbers not reported)	The review found no significant difference between groups in withdrawals (all causes [8 RCTs; RR 0.98, 95% CI 0.82 to 1.17], withdrawal due to adverse effects [4 RCTs; RR 1.11, 95% CI 0.75 to 1.6]), or any adverse effects (4 RCTs; RR 1.07, 95% CI 0.92 to 1.24). Alfuzosin significantly increased dizziness compared with placebo (6 RCTs; 68/1298 [5%] with alfuzosin *v* 25/1000 [3%] with placebo; RR 2.04, 95% CI 1.29 to 3.22)
[9] Systematic review (search date 2006)	Alfuzosin *v* placebo		See any alpha-blocker *v* placebo above	See any alpha-blocker *v* placebo above
[17] RCT	Sustained-release alfuzosin (5 mg twice daily for 48 hours) *v* placebo	81 men catheterised for acute urinary retention	**Proportion of men able to pass urine after catheter removal:** 22/40 (55%) with alfuzosin *v* 12/41 (29%) with placebo; OR 2.95, 95% CI 1.08 to 8.21	4 people had adverse effects with alfuzosin compared with no adverse effects with placebo. 1 person had fainting, 1 had dizziness, 1 headache, and 1 atrial fibrillation. No statistical information reported
[18] [21] RCT	Alfuzosin (10 mg/day) *v* placebo	First phase: 360 men (catheterised for acute urinary retention related to BPH) alfuzosin *v* placebo for 3 days [18] Second phase: 165 men (with successful passage of urine after catheter removal) alfuzosin *v* placebo for 6 months [21]	First phase: **Proportion of men who successfully passed urine after catheter removal and did not require recatheterisation:** 146/236 (62%) with alfuzosin *v* 58/121 (48%) with placebo; P = 0.012	Withdrawal due to adverse effects at 3 days: 1.7% with alfuzosin *v* 0.8% with placebo Withdrawal due to adverse effects at 6 months: 1.2% with alfuzosin *v* 4.8% with placebo; P values not reported
			Second phase: **Proportion of men requiring surgery for BPH at 6 months:** 14/82 (17%) with alfuzosin *v* 20/83 (24%) with placebo Using Kaplan–Meier analysis, the difference between groups was significant at 1 and 3 months, but not by 6 months (ARI of being surgery free: at 1 month: 9.6%, 95% CI 0.2% to 19.0%; P = 0.04; at 3 months: 11.4%, 95% CI 0.3% to 22.4%; P = 0.04; at 6 months: +8.3%, 95% CI –4.6% to +21.3%; P = 0.20)	Any adverse effect, at 3 days: 1.3% with alfuzosin *v* 1.6% with placebo; at 6 months: 4.8% with alfuzosin *v* 4.9% with placebo Vasodilation-related adverse effects, at 3 days: 6/238 (2.5%) with alfuzosin *v* 1/222 (0.5%) with placebo; at 6 months: no people with either treatment; P values not reported

Reference study type	Intervention	Population	Benefits	Harms
[20] RCT included in systematic review [9] (see any alpha-blocker *v* placebo above)	Alfuzosin 10 mg daily *v* placebo	1522 men "at risk of having progression of events from LUTS/BPH" Age 55 years or over Analysis based on 1506 men. Trial duration 2 years		**First episode of acute urinary retention:** 16/749 (2.1%) with alfuzosin *v* 14/757 (1.8%) with placebo; P = 0.82 **Risk of BPH-related surgery:** 38/749 (5%) with alfuzosin *v* 49/757 (6%) with placebo; RR +22%, 95% CI –18% to +48%; P = 0.18 **Overall risk of progression (worsening of IPSS score by 4 points or more):** 88/749 (12%) with alfuzosin *v* 127/757 (17%) with placebo; P = 0.0013 (post-hoc analysis) **Overall clinical progression (acute urinary retention and/or surgery and/or IPSS worsening of 4 points or more):** 122/747 (16%) with alfuzosin *v* 167/757 (22%) with placebo; RR 26%, 95% CI 9% to 40% (post-hoc analysis) Alfuzosin also significantly improved IPSS score (P = 0.017), quality of life (P <0.001), and peak flow rate (P = 0.001) compared with placebo

Reference study type	Intervention	Population	Benefits	Harms	
					The RCT reported that there was a similar incidence of serious adverse effects between groups (statistical analysis between groups not reported) 513 men discontinued the study mainly for lack of efficacy or disease progression (9.9% with alfuzosin *v* 4.6% with placebo). Dizziness was the most common adverse effect (6.0% with alfuzosin *v* 4.6% with placebo; statistical analysis between groups not reported). The incidence of hypotension/postural hypotension was 1.2% with alfuzosin *v* 0.5% with placebo, and incidence of ejaculation disorders was 0.4% with alfuzosin *v* 0% with placebo (statistical analysis between groups

Reference study type	Intervention	Population	Benefits	Harms	
					not reported) Mean change in systolic/diastolic BP: −3.2/−2.9 mmHg while supine and −3.8/−2.8 mmHg while standing with alfuzosin and −0.1/−0.8 mmHg while supine and −0.2/−0.5 mmHg while standing with placebo
[19] RCT	Extended-release alfuzosin *v* placebo	372 men aged 50 years or above, LUTS associated with BPH for 6 months or longer 4-week placebo run-in period and 4-week treatment period after which outcomes were assessed At baseline, 64% of men had erectile dysfunction and 63% had ejaculatory dysfunction measured using DAN-PSSsex score	**Erectile function:** Erectile function significantly improved with alfuzosin compared with placebo at day 29 (absolute numbers not reported, results presented graphically; P = 0.02). For subgroup with erectile dysfunction at baseline, no significant difference between groups at day 29 (P = 0.09) **Ejaculatory function:** No significant difference between groups in ejaculatory function at day 29 (absolute numbers not reported, results presented graphically; P = 0.31). For subgroup with ejaculatory dysfunction at baseline, improvements reported as "comparable" between groups (−0.16 with alfuzosin *v* −0.15 with placebo; statistical analysis between groups not reported) Results based on 320/372 (86%) of men who completed the questionnaire	Percentage of men with treatment-emergent adverse effects: 25% with alfuzosin *v* 23% with placebo; statistical analysis between groups not reported. Dizziness was the most common adverse effect reported (11/185 [5%] with alfuzosin *v* 0/185 [0%] with placebo; statistical analysis between groups not reported). Other individual adverse effects occurred in 3% or less in each group	
Doxazosin *v* placebo					
[9] Systematic review (search date 2006)	Doxazosin *v* placebo		See any alpha-blocker *v* placebo above	See any alpha-blocker *v* placebo above	
Silodosin *v* placebo or tamsulosin					

Reference study type	Intervention	Population	Benefits	Harms
[22] RCT	Silodosin 4 mg twice daily *v* placebo or tamsulosin 0.2 mg daily (note: usual tamsulosin dose in Europe and North America is 0.4 mg/day)	457 Japanese men 50 years or older (silodosin, 176 men; tamsulosin, 192 men; placebo, 89 men)	Change in total IPSS score from baseline at 12 weeks: −8.3 with silodosin *v* −6.8 with tamsulosin *v* −5.3 with placebo. Change in urinary flow (Qmax) from baseline: 2.24 mL/second with silodosin *v* 2.95 mL/second with tamsulosin *v* 2.42 mL/second with placebo Silodosin significantly improved total IPSS score from baseline compared with placebo (−3.0, 95% CI −4.6 to −1.3) and tamsulosin (−1.4, 95% CI −2.7 to −0.2) No significant difference among groups in urinary flow (Qmax; reported as no significant difference; P value not reported) Change in QoL score from baseline: −1.7 with silodosin *v* −1.4 with tamsulosin *v* −1.1 with placebo. Silodosin significantly better than placebo (P = 0.002) Analysis of tamsulosin *v* placebo not reported for IPSS score, urinary flow, or QoL score	Incidence of drug-related adverse events: 69.7% with silodosin *v* 47.4% with tamsulosin *v* 36.4% with placebo, with a significantly increased frequency with silodosin than with placebo or tamsulosin (P <0.001; other statistical analysis between groups not reported) Abnormal ejaculation was more common with silodosin (22.3%) than with tamsulosin (1.6%) or placebo (0%; statistical analysis between groups not reported) Dizziness: 5.1% with silodosin *v* 7.3% with tamsulosin *v* 4.5% with placebo (statistical analysis between groups not reported)
Tamsulosin *v* other alpha-blockers				
[10] Systematic review (search date 2000)	Tamsulosin *v* other alpha-blockers	5 RCTs, 748 men	The review did not pool the results for comparisons between tamsulosin and all other alpha-blockers **Tamsulosin 0.2 mg daily *v* terazosin 2 mg to 5 mg:** WMD for change in IPSS: 4 RCTs; –0.72 points, 95% CI –2.54 points to +1.51 points WMD for change in peak urine flow: –0.26 mL/second, 95% CI –1.12 mL/second to +0.60 mL/second **Tamsulosin *v* alfuzosin:** Improvement in Boyarsky Symptom Score; 1 RCT; about 40% in each group Peak urine flow: about 16% in each group **Tamsulosin *v* prazosin:** Improvement in IPSS score: 1 RCT; 26% with tamsulosin *v* 38% with prazosin Improvement in peak urine flow: 15% with tamsulosin *v* 27% with prazosin; P values reported as non-significant; CI not reported	**Tamsulosin *v* terazosin:** Discontinuation of treatment because of adverse effects: 4 RCTs; RR for tamsulosin *v* terazosin 0.15, 95% CI 0.04 to 0.57 **Tamsulosin *v* alfuzosin:** All-cause withdrawal from treatment: 1 RCT; RR 1.46, 95% CI 0.66 to 3.25 Dizziness: 1 RCT; AR 6.8% with tamsulosin *v* 7.3% with alfuzosin; RR 0.94, 95% CI 0.39 to 2.29 Asthenia: 1 RCT; AR 3% with tamsulosin *v* 1.6% with alfuzosin; RR 1.88, 95% CI 0.35 to 10.08 Headache: 1 RCT; AR 7.6% with tamsulosin *v* 3.2% with alfuzosin; RR 2.35, 95% CI 0.76 to 7.29 **Tamsulosin *v* prazosin:** All-cause withdrawal from treatment: 1 RCT; RR 2.87, 95% CI 0.65 to 12.65 Risk of abnormal ejaculation increased with increasing dose of tamsulosin (0% with 0.2 mg/day *v* 18% with 0.8 mg/day; CI not reported)
[12] Systematic review (search date 2001)	Terazosin *v* other alpha-blockers	4 RCTs, 492 men	**Terazosin *v* tamsulosin:** IPSS scores: improvement: 40% with terazosin *v* 41% with tamsulosin; WMD of IPSS score: +0.72 points, 95% CI –1.51 points to +2.93 points Increase in peak flow rate: 25% with terazosin *v* 29% with tamsulosin; WMD +0.26%, 95% CI –0.60% to +1.12%	**Terazosin *v* tamsulosin:** Discontinuation because of adverse effects: 7.4% with terazosin *v* <1% with tamsulosin; RR 6.88, 95% CI 1.83 to 25.91

Reference study type	Intervention	Population	Benefits	Harms
[23] Crossover RCT	Tamsulosin *v* doxazosin GITS (gastrointestinal therapeutic system, extended-release) Treated in 4 phases: placebo run-in for 2 weeks; first study drug doxazosin-GITS or tamsulosin for 8 weeks; washout with placebo for 2 weeks; second study drug tamsulosin or doxazosin-GITS for 8 weeks. Doxazosin-GITS was started at 4 mg daily and tamsulosin at 0.4 mg daily, and then titrated to 8 mg daily and 0.8 mg daily, respectively, after 4 weeks of therapy if the increase in Qmax was <3 mL/second or the reduction in total IPSS was <30%	52 men aged 50 to 80 years with concomitant BPH and hypertension (with a diastolic blood pressure of at least 90 mmHg at the initial screening) Analysis based on 47/52 (90%) men	**IPSS:** Doxazosin-GITS produced significantly greater improvements from baseline than tamsulosin in total IPSS score (16.4 to 8.2 with doxazosin *v* 16.1 to 9.8 with tamsulosin; P = 0.019) **Obstructive subscores:** Doxazosin-GITS also significantly improved obstructive subscores (P = 0.004) at the last visit **Urinary flow:** No significant difference between groups in urinary flow (Qmax, change: 2.6 mL/second with doxazosin-GITS *v* 1.7 mL/second with tamsulosin; P = 0.089)	Treatment-related adverse effects seen included: dizziness (8% with doxazosin GITS *v* 8% with tamsulosin); headache (6% with doxazosin GITS *v* 8% with tamsulosin); asthenia (6% with doxazosin GITS *v* 12% with tamsulosin); somnolence (4% with doxazosin GITS *v* 2% with tamsulosin); hypotension (4% with doxazosin GITS *v* 2% with tamsulosin); rhinitis (2% with doxazosin GITS *v* 4% with tamsulosin); retrograde ejaculation (0% with doxazosin GITS *v* 2% with tamsulosin); statistical analysis between groups not reported
[24] RCT	Tamsulosin *v* naftopidil 31 men receiving naftopidil 50 mg daily, and 28 men receiving tamsulosin 0.2 mg once daily (note: usual tamsulosin dose in Europe and North America is 0.4 mg/day)	59 Japanese men with LUTS due to BPH	**IPSS and urinary flow:** No significant difference between groups for total IPSS score at 2 weeks (P = 0.43) or 6 to 8 weeks (P = 0.98). No significant difference between groups in urinary flow at 6 to 8 weeks (P = 0.46) **Storage symptoms:** Compared with tamsulosin, naftopidil significantly improved storage symptoms at 2 weeks (combined score of daytime frequency and nocturia; P = 0.0489)	Adverse effects not reported
[25] Crossover RCT	Tamsulosin *v* naftopidil 17 men initially prescribed naftopidil 50 mg for 4 weeks, followed by tamsulosin 0.2 mg for 4 weeks (group A), and another 17 were prescribed tamsulosin 0.2 mg, followed by naftopidil 50 mg (group B). The men crossed over to the alternative after a 1-week washout period (note: usual tamsulosin dose in Europe and North America is 0.4 mg/day)	34 Japanese men (mean age 72.4 years; prostate volume 19.8 mL) with LUTS secondary to BPH. Men with a total IPSS of <7 or a maximum urinary flow rate (Qmax) of >15 mL/second were excluded	**IPSS:** No significant difference between groups in IPSS (baseline to final assessment: 20.4 to 9.3 with tamsulosin *v* 20.4 to 8.9 with naftopidil; P = 0.265) **Storage symptoms:** Naftopidil was significantly more effective than tamsulosin in relieving storage symptoms (P <0.01) and especially nocturia (P <0.001) **Bladder outflow obstruction:** Both agents reduced bladder outflow obstruction according to pressure flow studies (23/34 [67%] with naftopidil *v* 23/34 [67%] with tamsulosin) **Urinary flow:** No significant difference between groups in peak urinary flow (Qmax; P = 0.136)	Adverse effects not reported

Reference study type	Intervention	Population	Benefits	Harms
[26] RCT	Tamsulosin *v* doxazosin GITS (gastrointestinal therapeutic system, extended-release)	165 Brazilian men with BPH (>50 years and IPSS >12) Analysis based on 158/165 (96%) men	**IPSS and urinary flow:** No significant difference between groups in IPSS at 12 weeks (absolute results not reported, results presented graphically; P = 0.759) or peak urinary flow (Qmax; P = 0.526) Improvement with doxazosin-GITS seemed more rapid than with tamsulosin over weeks 4 to 8 (based on baseline data and asking men how satisfied they were with treatment)	Tamsulosin significantly reduced the proportion of men reporting little or no difficulty ejaculating compared with doxazosin (71.3% with tamsulosin *v* 87.1% with doxazosin GITS; P = 0.018)
Terazosin *v* other alpha-blockers				
[12] Systematic review (search date 2001)	Terazosin *v* other alpha-blockers	See results	**Terazosin *v* tamsulosin:** See tamsulosin, above **Terazosin *v* alfuzosin:** Improvement in IPSS score (1 RCT, 74 men): 51% with terazosin *v* 48% with alfuzosin; P = 0.29 **Terazosin *v* doxazosin:** Improvement in Boyarsky Symptom Score (1 RCT, 43 men): 38–47% with terazosin *v* 42% with doxazosin; P value not reported **Terazosin *v* prazosin:** Improvement in IPPS score (1 RCT, 121 men): 39% with terazosin *v* 38% with prazosin; P value not reported	**Terazosin *v* tamsulosin:** See tamsulosin, above **Terazosin *v* alfuzosin:** Dizziness: 1 RCT; 5.1% with terazosin *v* 0% with alfuzosin; RR 4.50, 95% CI 0.22 to 90.64 **Terazosin *v* doxazosin:** Discontinuation rates: 1 RCT; RR 1.75, 95% CI 0.48 to 6.41 Dizziness: 1 RCT; 14.3% with terazosin *v* 4.5% with doxazosin; RR 3.14, 95% CI 0.35 to 27.88 Headache: 1 RCT; 4.8% with terazosin *v* 4.5% with doxazosin; RR 1.05, 95% CI 0.07 to 15.69 **Terazosin *v* prazosin:** Discontinuation rate: 1 RCT; RR 3.93, 95% CI 0.92 to 16.72 These analyses may have lacked power to exclude a clinically important effect
Alfuzosin *v* other alpha-blockers				
[10] Systematic review (search date 2000)	Alfuzosin *v* tamsulosin	1 RCT	See tamsulosin *v* other alpha-blockers, above	See tamsulosin *v* other alpha-blockers, above
[27] RCT	Alfuzosin *v* prazosin	103 men	**Boyarsky Symptom Score at 21 days:** Change in symptom score: –2.6 with alfuzosin *v* –2.8 with prazosin; P value not reported	4 people had adverse effects with prazosin (all 4 related to decrease in blood pressure) and 4 had adverse effects with alfuzosin (1 related to decrease in blood pressure)
[28] RCT	Alfuzosin (5–10 mg two or three times daily; mean dose at end point 8.8 mg/day) *v* doxazosin (1–8 mg once daily; mean dose at end point 6.1 mg/day) over 14 weeks	210 men	The mean doses of the medications used were not equivalent **Total IPPS:** Change in total IPPS: –9.2 with doxazosin *v* –7.5 with alfuzosin; P = 0.036 **Irritative IPPS:** Change: –3.5 with doxazosin *v* –2.8 with alfuzosin; P = 0.049	Withdrawals due to adverse effects: 12/99 (12%) with doxazosin *v* 7/93 (8%) with doxazosin Any adverse effect: 50.5% with alfuzosin *v* 48.5% with doxazosin Dizziness: 12% with alfuzosin *v* 14% with doxazosin Serious adverse effects: 4.3% with alfuzosin *v* 2.0% with doxazosin; P values not reported
Doxazosin *v* other alpha-blockers				

Reference study type	Intervention	Population	Benefits	Harms
[12] Systematic review (search date 2001)	Doxazosin *v* terazosin	1 RCT, 43 men	See terazosin *v* other alpha-blockers, above	See terazosin *v* other alpha-blockers, above
[28] RCT	Doxazosin (mean dose 6.1 mg/day) *v* alfuzosin (mean dose 8.8 mg/day) over 14 weeks	210 men	See alfuzosin *v* other alpha-blockers, above	See alfuzosin *v* other alpha-blockers, above
[29] Two RCTs combined in a single analysis	Standard doxazosin *v* controlled-release doxazosin 1 of the RCTs included a placebo-controlled group [72]	1475 men	**IPSS improvement from baseline:** –7.9 points with controlled release *v* –8.0 points with standard; adjusted mean difference –0.1 points, 95% CI –0.5 points to +0.3 points	A similar proportion of men reported adverse effects with both formulations. The most common adverse effects were headache, dizziness, respiratory tract infection, and asthenia. No further details were reported
Prazosin *v* other alpha-blockers				
[10] Systematic review (search date 2000)	Prazosin *v* tamsulosin	1 RCT	See tamsulosin *v* other alpha-blockers above	See tamsulosin *v* other alpha-blockers, above
[12] Systematic review (search date 2001)	Prazosin *v* terazosin	1 RCT, 121 men	See terazosin *v* other alpha-blockers above	See terazosin *v* other alpha-blockers, above
Terazosin *v* 5 alpha-reductase inhibitors				
[12] Systematic review (search date 2001)	Terazosin *v* 5 alpha-reductase inhibitors The identified RCT compared terazosin (10 mg/day), finasteride (5 mg/day), and terazosin plus finasteride	The RCT (1229 men) [14] identified by the review [12] was of poor quality and was limited by low drug doses, and unclear methods of randomisation and blinding	**Terazosin *v* finasteride:** AUA-SI score: Mean change in AUA-SI score: –6.1 points with terazosin *v* –3.2 points with finasteride; WMD –2.80 points, 95% CI –3.88 points to –1.72 points; P <0.001	Terazosin *v* finasteride (significance not reported for any comparison): Dizziness: 26% with terazosin *v* 8% with finasteride Generalised weakness: 14% with terazosin *v* 7% with finasteride Rhinitis: 7% with terazosin *v* 3% with finasteride Postural hypotension: 8% with terazosin *v* 2% with finasteride Impotence: 9% with finasteride *v* 6% with terazosin
Alfuzosin *v* 5 alpha-reductase inhibitors				
[30] RCT	Alfuzosin *v* finasteride *v* alfuzosin plus finasteride for 6 months	1051 men	**Alfuzosin *v* finasteride:** Change in IPSS score: –6.3 points with alfuzosin *v* –5.2 points with finasteride; P = 0.01	The RCT gave no information on adverse effects
Doxazosin *v* 5 alpha-reductase inhibitors				

Reference study type	Intervention	Population	Benefits	Harms
[31] RCT	Doxazosin *v* finasteride *v* doxazosin plus finasteride *v* placebo	1095 men	**Doxazosin *v* finasteride alone:** Total IPSS at 1 year: mean endpoint IPSS 8.7 with doxazosin *v* 10.9 with finasteride; P <0.05 Peak urinary flow rate over 1 year: mean endpoint Qmax 14.0 mL/second with doxazosin *v* 12.1 mL/second with finasteride **Doxazosin plus finasteride *v* finasteride alone:** Total IPPS at 1 year: mean endpoint IPSS 8.7 with doxazosin *v* 10.9 with finasteride; P <0.05 Peak urinary flow rate: mean endpoint Qmax 14.5 mL/second *v* 12.1 mL/second with finasteride; P <0.05	Discontinuing treatment because of adverse effects: 11.6% with doxazosin *v* 13.6% with finasteride; significance not reported Asthenia: 10.5% with doxazosin *v* 4.2% with finasteride; P <0.05 Dizziness: 15.6% with doxazosin *v* 8.0% with finasteride; P <0.05 Hypotension: 5.1% with doxazosin *v* 0.8% with finasteride; P <0.05
[32] RCT	Doxazosin *v* finasteride *v* doxazosin plus finasteride *v* placebo	3047 men	**Clinical progression (per 100 person-years):** 2.7 men with doxazosin *v* 2.9 men with finasteride; reported as not significant **AUA-SI:** Mean change at 4 years: –6.6 with doxazosin *v* –5.6 with finasteride; P = 0.001	Adverse effects (rate per 100 person-years) doxazosin *v* finasteride: Erectile dysfunction: 3.56 with doxazosin *v* 4.53 with finasteride Dizziness: 4.41 with doxazosin *v* 2.33 with finasteride Postural hypotension: 4.03 with doxazosin *v* 2.56 with finasteride Asthenia: 4.08 with doxazosin *v* 1.56 with finasteride Decreased libido: 1.56 with doxazosin *v* 2.36 with finasteride Statistical comparisons between these groups not reported
Tamsulosin *v* 5 alpha-reductase inhibitors				
[33] RCT	Tamsulosin *v* finasteride	205 men	**IPPS:** Mean change at 4 weeks: –3.5 with tamsulosin *v* –1.9 with finasteride; P <0.05 Mean change at 24 weeks: –6.9 with tamsulosin *v* –5.8 with finasteride; P reported as not significant **Peak flow rate:** Mean at 4 weeks: +1.0 mL/second with tamsulosin *v* +0.3 mL/second with finasteride; P <0.05 Mean at 24 weeks: +2.2 mL/second with tamsulosin *v* +2.2 mL/second with finasteride; P value reported as not significant, CI not reported	The RCT gave no information on adverse effects
[34] RCT	Tamsulosin (0.4 mg once daily) *v* finasteride (5 mg once daily) for 1 year	403 men	**Urinary flow at 12 weeks:** 2.3 mL/second with tamsulosin *v* 0.7 mL/second with finasteride; P = 0.0007	Adverse effects: 29.4% with finasteride *v* 32.1% with tamsulosin; P value not reported The most common adverse effects (reported in >3.0% of men) were: Impotence: 3.4% with finasteride *v* 6.1% with tamsulosin Abdominal pain: 2.5% with finasteride *v* 3.1% with tamsulosin Ejaculation disorder: 1.0% with finasteride *v* 3.1% with tamsulosin P values not reported

Reference study type	Intervention	Population	Benefits	Harms
[35] RCT	Dutasteride 0.5 mg *v* tamsulosin 0.4 mg *v* the combination once daily for 4 years The primary end point at 2 years was the change in IPSS from baseline	4844 men aged 50 years or older with a clinical diagnosis of BPH by medical history and physical examination, including rectal examination, IPSS 12 points or greater, prostate volume 30 cc or greater, total serum prostate-specific antigen 1.5 ng/mL or greater to 10 ng/mL or less and peak urinary flow >5 to 15 mL per second or less with a minimum voided volume of 125 mL or greater Note: 3-armed trial; 1623 men with dutasteride alone; 1611 men with tamsulosin alone	**IPSS and flow rate:** Change from baseline to 2 years in mean IPSS score: 4.9 with dutasteride *v* 4.3 with tamsulosin; P = 0.0113. Change from baseline to 2 years in flow rate (increase in Qmax: 1.9 mL/second with dutasteride *v* 0.9 mL/second with tamsulosin; P <0.0001)	The RCT found similar numbers of any adverse effects (64 with dutasteride *v* 63 with tamsulosin), any serious adverse effect (12 with dutasteride *v* 13 with tamsulosin), or any drug-related adverse effect (18 with dutasteride *v* 16 with tamsulosin) between groups (statistical analysis between groups not reported)
[36] Subgroup analysis of larger RCT [35]	Dutasteride 0.5 mg *v* tamsulosin 0.4 mg *v* the combination once daily for 4 years The primary end point at 2 years was the change in IPSS from baseline	325 men who defined their ethnicity as Asian This was a post-hoc analysis	**IPSS and flow rate:** Change from baseline to 2 years in mean IPSS score: 6.3 with dutasteride *v* 4.5 with tamsulosin; statistical analysis between groups not reported. Change from baseline to 2 years in flow rate (Qmax: 0.9 mL/second with dutasteride *v* 0.2 mL/second with tamsulosin; statistical analysis between groups not reported	The analysis found similar rates of adverse effects (76% with dutasteride *v* 79% with tamsulosin) and severe adverse effects (17% with dutasteride *v* 18% with tamsulosin; statistical analysis between groups not reported)

AUA-SI, American Urological Association Symptom Index; BPH, benign prostatic hyperplasia; GITS, Gastrointestinal Therapeutic System; IPSS, International Prostate Symptom Score; LUTS, lower urinary tract symptoms; QoL, quality of life.

TABLE 2 Transurethral resection

Reference	Population	Benefits	Harms
Transurethral resection (TURP) *v* watchful waiting			
[56] [58] RCT	556 men with moderate symptoms of BPH	At 3 years: Mean urinary symptom score (score range 0–27, higher score = greater severity): 4.9 with TURP *v* 9.1 with watchful waiting; P <0.001 Mean peak urinary flow rate: 17.8 mL/second with TURP *v* 12.7 mL/second with watchful waiting; P <0.001 At 5 years: Treatment failure rate: 10% with TURP *v* 21% with watchful waiting; NNT 9, 95% CI 7 to 17 36% of men assigned to watchful waiting crossed over to surgery (Treatment failure defined as death, acute urinary retention, high residual urine volume, renal azotaemia, bladder stones, persistent incontinence, or symptom score >14)	No increase in erectile dysfunction or incontinence with TURP compared with watchful waiting (P values not reported)
[57] [59] RCT (3-arm trial including a non-contact laser prostatectomy comparator group)	340 men (223 in TURP or watchful waiting groups)	At 7.5 months: Mean difference in IPSS: 10.4 points, 95% CI 8.5 points to 12.3 points	Adverse effects after TURP included blood transfusion (1/117 [1%]), septicaemia (2/117 [2%]), urinary tract infection (2/117 [2%]), and prostatic capsule perforation (2/117 [2%]). TURP *v* watchful waiting: Erectile dysfunction: OR 0.37, 95% CI 0.19 to 0.74 Pain or discomfort on ejaculation: OR 0.06, 95% CI 0.01 to 0.49 Ejaculatory dysfunction: OR 3.27, 95% CI 1.69 to 6.35
Transurethral resection *v* transurethral incision (TUIP):			
[60] Systematic review (search date 1999)	9 RCTs	Symptom scores at 12 months: 4 RCTs, 243 men; WMD +0.2 points, 95% CI –0.8 points to +1.1 points	Adverse effects with TURP *v* TUIP: Complications: 56/159 (35%) with TURP *v* 31/155 (20%) with TUIP Retrograde ejaculation: 52/72 (72%) with TURP *v* 14/67 (21%) with TUIP Blood transfusion: 58/231 (25%) with TURP *v* 2/230 (1%) with TUIP Significance of difference between groups not reported
[61] Systematic review (search date 2006)	11 RCTs	Symptom scores at 12 months: 6 RCTs reporting IPSS/AUA scores. Results not pooled as data not presented in a way that allowed analysis. No clear pattern emerged. 3 RCTs tended to favour TURP, 1 RCT tended to favour TUIP, and 2 RCTs found no difference Flow rate (Qmax) at 3 months: 3 RCTs, 124 men; WMD –0.07 mL/second, 95% CI –3.53 mL/second to +3.39 mL/second; P = 0.97	Adverse effects: No significant difference between TUIP and TURP in urinary retention (4 RCTs, 413 men; RR 1.84, 95% CI 0.70 to 4.86), or mortality (6 RCTs, 605 men; RR 1.22, 95% CI 0.64 to 2.32) Significantly fewer transfusions with TUIP compared with TURP (3/266 [1%] with TUIP *v* 77/272 [28%] with TURP; RR 0.06, 95% CI 0.03 to 0.16; P <0.00001) No significant difference between groups in urinary incontinence (3 RCTs, 328 men; RR 0.47, 95% CI 0.14 to 1.65; P = 0.24) Re-operations significantly more common with TUIP compared with TURP (7 RCTs, 467 men; RR 1.87, 95% CI 1.16 to 3.03; P = 0.01)
Transurethral resection *v* visual laser ablation/laser vaporisation			

Reference	Population	Benefits	Harms
[62] Systematic review (search date 2002)	8 RCTs, 1024 men	Mean AUA-SI score at 6 to 12 months: 4 RCTs, 236 men; WMD +0.21, 95% CI –2.28 to +2.70 Change in AUA-SI symptoms score from baseline to >6 months: 3 RCTs, 359 men; WMD –2.47, 95% CI –4.24 to –0.70 (favouring TURP) Mean peak urine flow from baseline to >6 months (mL/second): 4 RCTs, 236 men; WMD 2.64, 95% CI 0.53 to 4.75 (favouring TURP) Mean change in peak urine flow from baseline to >6 months (mL/second): 3 RCTs, 385 men; WMD 3.18, 95% CI 1.47 to 4.89 (favouring TURP)	Acute urinary retention: 4 RCTs, 311 men; RR 0.28, 95% CI 0.17 to 0.69 Urinary tract infection: 6 RCTs, 678 men; RR 0.45, 95% CI 0.21 to 0.98 Dysuria: 4 RCTs, 362 men; RR 0.28, 95% CI 0.08 to 1.00
[63] Longer-term follow-up of 1 RCT included in review [62]	98 men	5-year surgical re-treatment rates: 18/47 (38%) with visual laser ablation *v* 8/51 (16%) with TURP; P = 0.006	The RCT gave no information on adverse effects
[61] Systematic review (search date 2006)	11 RCTs	**Symptom improvement (IPSS/AUA scores)** 3 months: 3 RCTs, 197 men; WMD –0.01, 95% CI –1.39 to +1.36 (significant heterogeneity among RCTs; P = 0.004) 6 months: 3 RCTs, 149 men; WMD +0.27, 95% CI –1.01 to +1.54 (significant heterogeneity among RCTs; P = 0.01) 12 months: 4 RCTs, 183 men, WMD 1.30, 95% CI 0.12 to 2.47 (in favour of TURP) 2 years: 2 RCTs, 139 men; WMD +1.77, 95% CI –0.16 to +3.70 5 years: 2 RCTs, 119 men; WMD 2.42, 95% CI 0.08 to 4.75 (in favour of TURP) **Flow rates (Qmax; mL/second)** 3 months: 4 RCTs, 304 men; WMD –1.76, 95% CI –2.94 to –0.57 (in favour of TURP) 6 months: 3 RCTs, 206 men; WMD –1.51, 95% CI –2.55 to –0.47 (in favour of TURP) 12 months: 2 RCTs, 160 men; WMD –2.02, 95% CI –4.75 to +0.71 2 years: 2 RCTs, 100 men; WMD –0.44, 95% CI –3.10 to +2.23 5 years: 2 RCTs, 119 men; WMD –0.28, 95% CI –2.32 to +1.76	Urinary retention: 6 RCTs, 610 men; RR 2.89, 95% CI 1.55 to 5.42 (in favour of TURP) Blood transfusion: 10 RCTs, 789 men; RR 0.14, 95% CI 0.05 to 0.42 (in favour of laser) Re-operations: Of borderline significance in favour of TURP (8 RCTs, 678 men; RR 1.60, 95% CI 0.97 to 2.63; P = 0.06; note: differences in timing and follow-up may have introduced bias to this result)
Transurethral resection *v* contact laser ablation			
[62] Systematic review (search date 2002)	8 RCTs with minimum follow-up of 6 months, 851 men	**TURP *v* Nd:YAG contact laser:** IPSS symptom score: 3 RCTs, 227 men; WMD –1.78, 95% CI –3.22 to –0.35 (in favour of TURP) Peak urine flow (mL/second): 5 RCTs, 254 men; WMD +1.72, 95% CI –0.32 to +3.76 **TURP *v* Holmium contact laser:** IPSS symptom score: 1 RCT, 102 men; WMD +0.10, 95% CI –1.88 to +2.08 Peak urine flow (mL/second): 1 RCT, 102 men; WMD –4.8, 95% CI –8.79 to –0.81 (in favour of Holmium contact laser)	Urinary retention: 4 RCTs, 344 men; RR 1.97, 95% CI 0.68 to 5.72 Urinary tract infection: 3 RCTs, 332 men; RR 0.67, 95% CI 0.28 to 1.58 Retrograde ejaculation: 4 RCTs, 213 men; RR 1.58, 95% CI 0.36 to 6.94 Erectile dysfunction: 2 RCTs, 156 men; RR 0.87, 95% CI 0.27 to 2.80

BPH, benign prostatic hyperplasia; IPSS, International Prostate Symptom Score; TUIP, transurethral incision of the prostate; TURP, transurethral resection of the prostate.

TABLE **GRADE evaluation of interventions for benign prostatic hyperplasia**

Important outcomes			Symptom improvement, adverse effects						
Number of studies (participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
What are the effects of medical treatments in men with benign prostatic hyperplasia?									
Unclear (unclear) [9]	Symptom improvement	Alpha-blockers as a group *v* placebo	4	−1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
At least 7 (at least 2899) [10] [9] [11]	Symptom improvement	Tamsulosin *v* placebo	4	−1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
At least 7 (unclear) [12] [9]	Symptom improvement	Terazosin *v* placebo	4	−1	0	−1	0	Low	Quality point deducted for incomplete reporting of results. Directness point deducted for no direct statistical analysis between groups in 1 review
At least 11 (at least 3708) [16] [9] [17] [18] [19]	Symptom improvement	Alfuzosin *v* placebo	4	−1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
At least 6 (unclear) [9]	Symptom improvement	Doxazosin *v* placebo	4	−1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
1 (457) [22]	Symptom improvement	Silodosin *v* placebo	4	−1	0	−1	0	Low	Quality point deducted for incomplete reporting. Directness point deducted issues of generalisability (dosage of tamsulosin used; no statistical analysis for some outcomes)
At least 10 RCTs (at least 1048 men) [10] [12] [22] [23] [24] [25] [26]	Symptom improvement	Tamsulosin *v* other alpha-blockers	4	−2	0	0	0	Low	Quality points deducted for incomplete reporting of results and weak methods (alternate allocation in 1 RCT, crossover RCTs, lower dose of tamsulosin used in some RCTs)
7 (730) [12]	Symptom improvement	Terazosin *v* other alpha-blockers	4	−1	0	−1	0	Low	Quality point deducted for incomplete reporting of results. Directness point deducted for no statistical analysis between groups for some comparisons
3 (at least 313 men) [10] [27] [28]	Symptom improvement	Alfuzosin *v* other alpha-blockers	4	−1	0	−1	0	Low	Quality point deducted for incomplete reporting of results. Directness point deducted for comparing non-equipotent doses in 1 RCT
4 (463) [28] [29] [23] [26]	Symptom improvement	Doxazosin *v* other alpha-blockers	4	−1	0	−1	0	Low	Quality point deducted for incomplete reporting of results. Directness point deducted for comparing non-equipotent doses in 1 RCT
2 (at least 121 men) [10] [12]	Symptom improvement	Prazosin *v* other alpha-blockers	4	−1	0	−1	0	Low	Quality point deducted for incomplete reporting of results. Directness point deducted for no statistical analysis between groups in 1 RCT
1 (1229) [14]	Symptom improvement	Terazosin *v* 5 alpha-reductase inhibitors	4	−3	0	−1	0	Very low	Quality points deducted for uncertainty about methods of randomisation and blinding and for poor-quality RCT. Directness point deducted for comparing low doses
1 (1051) [30]	Symptom improvement	Alfuzosin *v* 5 alpha-reductase inhibitors	4	−1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results

Important outcomes			Symptom improvement, adverse effects						
Number of studies (participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
2 (unclear) [31] [32]	Symptom improvement	Doxazosin *v* 5 alpha-reductase inhibitors	4	−1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
3 (3842) [33] [34] [35] [36]	Symptom improvement	Tamsulosin *v* 5 alpha-reductase inhibitors	4	−1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
At least 19 (at least 11507) [42] [31] [32] [43] [42] [7] [44] [45] [46] [47]	Symptom improvement	5 alpha-reductase inhibitors *v* placebo	4	−1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
What are the effects of herbal treatments in men with benign prostatic hyperplasia?									
At least 10 (at least 1019) [40]	Symptom improvement	Saw palmetto plant extracts *v* placebo	4	−1	0	−1	0	Low	Quality point deducted for weak methods (RCTs mainly short term/lack of validated outcome measures). Directness point deducted for issues of generalisability (different preparations used, heterogeneity among RCTs, lack of RCTs at clinically relevant doses)
1 (704) [40]	Symptom improvement	Saw palmetto plant extracts *v* alpha-blockers	4	−2	0	0	0	Low	Quality points deducted for weak methods (allocation sequence generation/allocation concealment) and no intention-to-treat analysis
1 (1098) [40]	Symptom improvement	Saw palmetto plant extracts *v* 5 alpha-reductase inhibitors	4	−2	0	0	0	Low	Quality points deducted for loss to follow-up (13%) and no intention-to-treat analysis
2 (unclear) [53]	Symptom improvement	Beta-sitosterol plant extract *v* placebo	4	−2	0	−1	0	Very low	Quality points deducted for incomplete reporting of results and for short follow-up. Directness point deducted for uncertainty about generalisability of results due to lack of standardised preparations
2 (163) [54]	Symptom improvement	Rye grass pollen extract *v* placebo	4	−3	0	−1	+1	Very low	Quality points deducted for incomplete reporting of results, for short follow-up, and for uncertainty about allocation concealment. Directness point deducted for uncertainty about generalisability of results due to lack of standardised preparations. Effect size point added for RR 2–5
At least 5 RCTs (at least 430) [55]	Symptom improvement	*Pygeum africanum v* placebo	4	−2	0	−1	0	Very low	Quality points deducted for incomplete reporting of results and for short follow-up. Directness point deducted for uncertainty about generalisability of results due to lack of standardised preparations and variations in RCT designs
What are the effects of surgical treatments in men with benign prostatic hyperplasia?									
2 in 4 publications (779) [56] [57] [58] [59]	Symptom improvement	TURP *v* watchful waiting	4	0	0	0	0	High	
At least 11 (at least 243) [60] [61]	Symptom improvement	TURP *v* transurethral incision	4	−1	0	−1	0	Low	Quality point deducted for incomplete reporting of results. Directness point deducted for issues of generalisability (evidence may not be representative of current TURP outcomes)

Important outcomes			Symptom improvement, adverse effects						
Number of studies (participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
At least 4 (at least 385) [62] [61]	Symptom improvement	TURP *v* visual laser ablation/laser vaporisation	4	0	−1	−1	0	Low	Consistency point deducted for statistical heterogeneity among RCTs. Directness point deducted for results being dependent on type of analysis performed in 1 review
8 (851) [62]	Symptom improvement	TURP *v* contact laser	4	0	−1	0	0	Moderate	Consistency point deducted for conflicting results
At least 5 (at least 562) [41] [61]	Symptom improvement	TUMT *v* sham treatment	4	−1	−1	0	0	Low	Quality point deducted for weak methods in some RCTs. Consistency point deducted for statistical heterogeneity among RCTs
1 (103) [41]	Symptom improvement	TUMT *v* alpha-blockers	4	−2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
At least 5 (at least 370) [41] [61]	Symptom improvement	TUMT *v* TURP	4	−1	−1	−1	0	Low	Quality point deducted for weak methods (randomisation/blinding). Consistency point deducted for statistical heterogeneity among RCTs. Directness point deducted for substantial loses to follow-up
4 (450) [61]	Symptom improvement	TUNA *v* TURP	4	−1	0	−1	0	Low	Quality point deducted for no intention-to-treat analysis. Directness point deducted for inconsistent results depending on outcome measured and timeframe assessed
At least 5 (at least 458) [61]	Symptom improvement	HoLEP *v* TURP	4	0	−1	0	0	Moderate	Consistency point deducted for statistical heterogeneity among RCTs
1 (150) [61]	Symptom improvement	HoLEP *v* TUEVP or TURP	4	−2	0	0	0	Low	Quality points deducted for sparse data and weak methods (randomisation, blinding)
At least 7 (at least 672) [61]	Symptom improvement	TUEVP *v* TURP	4	0	−1	0	0	Moderate	Consistency point deducted for statistical heterogeneity among RCTs

Type of evidence: 4 = RCT. Consistency: similarity of results across studies. Directness: generalisability of population or outcomes. Effect size: based on relative risk or odds ratio.
HoLEP, transurethral holmium laser resection/enucleation; TUEVP, transurethral electrovaporisation of the prostate; TUMT, transurethral microwave thermotherapy; TUNA, transurethral needle ablation; TURP, transurethral resection of the prostate.