Introduction

The prostate is a small gland at the neck of the bladder, surrounding the urethra. Benign prostatic hypertrophy (also referred to as benign prostatic hyperplasia or BPH) is a common condition in men caused by the enlargement of the prostate gland. The condition is not life threatening, but it can cause problems with urination (mainly with frequency and urge), and can have an impact on quality of life. Men develop BPH as they age, though less than half of those with BPH will be troubled by symptoms of the disease or require treatment.\(^1\) In the US, 25% of men will receive treatment for BPH by the age of 80.\(^2\)

A special section of the Bandolier evidence-based medicine web site summarizes a few of the many trials and systematic reviews of therapies for BPH (http://www.jr2.ox.ac.uk/bandolier/band11/b11-3.html), and a 1997 Therapeutics Letter discusses some of the main drug therapies for this condition.\(^3\) Options for treatment include “watchful waiting” (no treatment until the severity of symptoms warrants), drug therapies, herbal therapies, the use of different types of radiation to ablate prostatic tissue through heating, various surgical procedures and mechanical approaches.

A. Drug therapies

- Prazosin (Minipress®, generic)
- Alfuzosin hydrochloride (Xatral®)
- Terazosin (Hytrin®)
- Doxazosin (Cardura®)
- Finasteride (Proscar®)
- Tamsulosin (Flomax)

B. Herbal therapies (Phytotherapy)

- saw palmetto (Serenoa repens – a dwarf palm) and plant extracts containing beta-sitosterols, in various combinations (these go by various trade names in different countries, such as Permixon, Harzol, Tadenan, Cernilton (rye-grass pollen Secale cereale) and Azuprostat)
- *Pygeum africanum* (bark of the African prune tree).

C. Radiation – linked treatments

- transurethral microwave therapy/transurethral thermal therapy (TUMT, e.g. using a device called the Prostatron)
Treatments for Benign Prostatic Hypertrophy

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**PRE-ASSESSMENT**

A. Non-surgical approaches

- transurethral needle ablation (TUNA) – radiofrequency energy (heat therapy) administered via a needle in the urethra
- microwave uroplasty (Celsion™ low heat treatment)
- the use of high-intensity focused ultrasound (HIFU) (e.g. the Sonablate® system)
- interstitial laser coagulation of the prostate (ILC)

B. Medical approaches

- alpha-blockers
- 5-alpha reductase inhibitors
- 5-alpha reductase inhibitors with alpha-blockers

C. Hormonal approaches

- testosterone-steroid withdrawal
- diethylstilbestrol
- flutamide

D. Surgical removal of tissue

- transurethral resection of the prostate (TURP) – surgical removal of part of the prostate. This has been the most commonly-used treatment for BPH.
- open prostatectomy – surgical removal of the prostate via an incision in the abdomen or perineal area. This is typically reserved for men with prostates too large to permit TURP. A laparoscopic procedure has also been developed.
- transurethral incision of the prostate (TUIP) – via the penis, an incision is made in the tissue of the prostate to widen the opening of the urethra, removing a minimal amount of the prostate gland
- transurethral ultrasound-guided laser incision of the prostate (TULIP) - similar to TUIP, but the incisions are made with a laser
- transurethral electrovaporization (TUVP or TVP) – electrosurgical coagulation to remove prostatic tissue
- visual laser ablation of the prostate (VLAP) – the use of a laser to destroy the obstructing parts of the prostate
- laser contact vaporization of the prostate (LCV)

E. Mechanical approaches

- prostatic stents
- transurethral balloon dilatation (TUBD) – similar to balloon angioplasty, a balloon is inflated to widen the prostate channel. Most patients require further treatment within two years. This therapy is no longer recommended.

**Research Questions**

The questions surrounding treatments for BPH concern the safety, effectiveness and cost-effectiveness of the various therapies, in comparison to each other and to no treatment. The effect of these therapies, or no treatment, on quality-of-life is another key issue. As the Bandolier review points out:
**PRE-ASSESSMENT**

Treatments for Benign Prostatic Hypertrophy

**CCOHTA**

BPH affects the quality rather than the quantity of life. It is therefore the degree to which the patient’s symptoms bother him that will determine the need for therapy; the relative benefits and harms of each treatment option will help to determine their therapeutic preference.²

**Assessment Process**

Literature searches were conducted using the Cochrane Library, the CRD Databases (DARE, NHS EED and HTA), and health technology assessment agency and related websites. A broad search of PubMed, using the term “prostatic hyperplasia” and related terms, and limited to meta-analyses or clinical trials in human populations, published from 1998 to date, resulted in over 700 records.

**Summary of Findings**

Therapies for this condition have received a great deal of study, and several have been the subject of assessments by HTA agencies. Many of these reviews were conducted in the early-mid 1990s, including a 1996 CCOHTA assessment of the drug finasteride (Proscar)⁶⁻¹¹ The table below lists selected assessments and systematic reviews that have been published since 1998.

<table>
<thead>
<tr>
<th>Type of report</th>
<th>Title</th>
<th>Reference</th>
<th>Main findings</th>
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<tbody>
<tr>
<td>Drug therapies</td>
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<tr>
<td>Systematic reviews [in progress]</td>
<td>Cochrane Reviews on other drug therapies (alfuzosin and doxazosin) for BPH are currently underway.</td>
<td>In: The Cochrane Library, Issue 1, 2003. Oxford: Update Software.</td>
<td>- The available evidence suggests that terazosin improves urinary symptoms and flow measures associated with BPO. Effectiveness is superior to placebo or finasteride, similar to other alpha-blockers but less than TUMT. Adverse effects were generally mild but more frequent than other alpha-blockers and associated with between a 2-4 fold increase in treatment discontinuation.</td>
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## Treatments for Benign Prostatic Hypertrophy

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<tr>
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<td>A substantive amendment to this systematic review was last made on August 20, 2002.</td>
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<td>&quot;Tamsulosin provided a small to moderate improvement in urinary symptoms and flow compared to men receiving placebo in men with BPH. Effectiveness was similar to other alpha antagonists and increased only slightly with higher doses. Long-term effectiveness and ability to reduce complications due to BPH progression could not be determined. Adverse effects were generally mild but their frequency, including withdrawals, increased substantially with the higher doses that are generally available for treatment.&quot;</td>
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## Herbal therapies

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<td>A substantive amendment to this systematic review was last made on March 20, 2002.</td>
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<td>&quot;The evidence suggests that Serenoa repens provides mild to moderate improvement in urinary symptoms and flow measures. Serenoa repens produced similar improvement in urinary symptoms and flow compared to finasteride and is associated with fewer adverse events. The long term effectiveness, safety and ability to prevent BPH complications are not known.&quot;</td>
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## Systematic review

**Beta-sitosterols for benign prostatic hyperplasia** *(Cochrane Review)*


- A substantive amendment to this systematic review was last made on May 19, 1999.

- Available with a subscription to the Cochrane Library, or by purchase from the publisher. Abstract available: [http://www.update-software.com/abstracts/ab001043.htm](http://www.update-software.com/abstracts/ab001043.htm).

- “The evidence suggests non-glucosidic B-sitosterols improve urinary symptoms and flow measures. Their long term effectiveness, safety and ability to prevent BPH complications are not known.”

## Systematic review

**Cernilton for benign prostatic hyperplasia** *(Cochrane Review)*


- A substantive amendment to this systematic review was last made on March 31, 1998.

- Available with a subscription to the Cochrane Library, or by purchase from the publisher. Abstract available: [http://www.update-software.com/abstracts/ab001042.htm](http://www.update-software.com/abstracts/ab001042.htm).

- “The available evidence suggests Cernilton is well tolerated and modestly improves overall urologic symptoms including nocturia. Additional randomized placebo and active-controlled trials are needed to evaluate the long-term clinical effectiveness and safety of Cernilton.”

## Radiation – linked treatments

**HTA**

**TUNA – Transurethral needle ablation for BPH**


- “The method has been studied in a randomized controlled trial and in several non-controlled studies. The findings suggest that TUNA has few side effects and yields relatively good results on urinary obstructions in the short
|---------------------|-----------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|

- "Based on the evidence available, while safe and efficacious in the short term, the long term effectiveness and cost-effectiveness of TUNA has not been proven. MSAC therefore concludes that unrestricted Medicare Benefits Scheme funding of TUNA for the surgical management of symptomatic benign prostatic hyperplasia is not warranted at this time."
- TUNA may have a limited role as an alternative option for symptomatic BPH with the following restrictions: in men with moderate to severe lower urinary tract symptoms. A long-term follow up shows that 20% of those treated with TUNA require additional treatment within two years."
- There is little evidence on the short-term and long-term effectiveness, benefits to patients and costs associated with this treatment.
- Health economic assessments of the method are not available.
- The introduction of TUNA will likely have only a minor economic impact on health services.
- Further evidence from controlled trials with 3-5 years of follow-up is needed.
Treatments for Benign Prostatic Hypertrophy

**PRE-ASSESSMENT**

<table>
<thead>
<tr>
<th>Method Description</th>
<th>Reference</th>
<th>Notes</th>
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<tr>
<td>Microwave thermotherapy for benign prostatic hyperplasia</td>
<td>Stockholm: Swedish Council on Technology Assessment in Health Care; 2002. Available: <a href="http://www.sbu.se/admin/main/Showdoc/Showdoc_default.asp?id=1268&amp;page=first&amp;area=alert">http://www.sbu.se/admin/main/Showdoc/Showdoc_default.asp?id=1268&amp;page=first&amp;area=alert</a></td>
<td>- There is good evidence of beneficial effects of microwave thermotherapy in the short term, but only poor quality evidence available regarding the long term benefits of this treatment. “Since information concerning the long-term effects and costs of the method remains insufficient, it is essential to develop this knowledge within the framework of studies.”</td>
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<tr>
<td>Transurethral microwave therapy in benign prostatic hyperplasia</td>
<td>Traitement de l'hypertrophie bénigne de la prostate par thermothérapie micro-ondes transurétrale. Paris: CEDIT; 2001. Available in French: <a href="http://cedit.aphp.fr/servlet/siteCedit?Destination=rec0&amp;numArticle=00.03">http://cedit.aphp.fr/servlet/siteCedit?Destination=rec0&amp;numArticle=00.03</a></td>
<td>- There are still many uncertainties concerning the indications, in particular the criteria making for defining the success of treatment and the benefit to the patient. But it may be of benefit for patients who fail medical therapy or are contraindicated for surgery. CEDIT recommends waiting for the results of studies currently in progress concerning the new high short energy microwave treatments, before drawing conclusions re the diffusion of this technology.</td>
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### Treatments for Benign Prostatic Hypertrophy

**CCOHTA**

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| HTA | Transurethral microwave thermotherapy (TUMT) for benign prostatic hyperplasia (BPH) | Plymouth Meeting (PA): ECRI; 2000. Target report no 662. Available with a subscription or by purchase from: http://www.ecri.org. | -N/A |
| HTA | Microwave thermotherapy for benign prostatic hypertrophy | Bloomington (MN): Institute for Clinical Systems Improvement; 1998. Available: http://www.icsi.org/display_file.asp?Fileld=275. | - “Microwave thermotherapy is a safe procedure with somewhat different and possibly lower morbidity than TURP; some of the newer treatment protocols are associated with greater patient discomfort and morbidity.”
- Success rates with this procedure vary depending on the outcome measure used.
- There is limited information on the “durability” of microwave therapy. |
## Surgical removal of tissue

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<th>Study Type</th>
<th>Description</th>
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- It is inappropriate to compare TUMT with TURP. BPH is not life threatening and patients may be unwilling to accept the risks and complications associated with TURP.

- Project is at the editorial review stage.

- "In the first 12 months after surgery, transurethral prostatectomy offered an equivalent effectiveness to transurethral resection for the treatment of patients with suspected benign prostatic obstruction, who have a relatively small prostate. However, there was little evidence on the relative long-term effectiveness of the two treatments, 2 to 5 or 10 years after surgery. There does not appear to be a clear cut-off point for prostate size that leads to good results after transurethral prostatectomy."
## Conclusion

A review of all therapies for benign prostatic hypertrophy would be a massive undertaking. Treatments currently under investigation, such as microwave uroplasty, might be appropriate topics for review under the CCOHTA emerging health technologies program. Systematic reviews of some of the drug and herbal therapies have been completed or are underway by Cochrane Collaboration review groups. TUNA has been the subject of recent assessments by the Swedish Council on Health Technology Assessment (SBU) and the Australian Medicare Services Advisory Committee (MSAC). Perhaps, through consultation with urologists and representatives of the provincial health ministries, the most controversial or rapidly diffusing treatments could be identified for full assessment.

## References


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