Technology Assessment

Technology Assessment Program

Agency for Healthcare Research and Quality

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Treatments for Benign Prostatic Hyperplasia

August 2, 2004

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Prepared for:
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Executive Summary

Background

Benign prostatic hyperplasia (BPH) is a condition primarily of middle-aged and elderly men. The frequency of the condition increases with age, so it is found in the majority of very elderly men. Consequently, surgical and medical treatments for BPH are some of the most common therapies administered in all of medical practice. BPH is associated with bothersome lower urinary tract symptoms that may include urgency to urinate, frequent urination, weak stream, straining, and/or the sensation of incomplete bladder emptying. These symptoms affect quality of life and sleeping patterns. Medical therapy is available for BPH; however, this may have undesirable side-effects and may provide inadequate relief for more severe cases.

Open prostatectomy may be used for men with very large prostates, but has been largely replaced by transurethral resection of the prostate (TURP) as the gold standard for surgical treatment of BPH. Transurethral incision of the prostate (TUIP) is considered by some to be an alternative standard for men with small prostates. Devices and techniques similar to TURP are used for transurethral electrovaporization (TUEVP) and transurethral vaporization with resection of the prostate (TUVRP), and these newer techniques have come to be considered variations on the TURP standard.

However, the standard surgeries may be accompanied by undesirable complications of blood loss, transfusion and absorption of irrigation fluids and may result in side-effects such as retrograde ejaculation and incontinence. Therefore, there have been attempts to develop new surgical techniques that use lasers, as well as minimally invasive techniques with heat, microwaves, radiofrequencies, and ultrasound, with the intent of developing techniques that are less invasive than TURP (and thus have fewer complications and side-effects), but provide equivalent symptom relief. It is also desirable that these newer treatments have low retreatment rates. Thus, there are many types of outcomes to examine in comparing these less invasive treatments to TURP. For these less invasive treatments, it may not be a simple question of comparative efficacy with TURP, but rather a question of whether lower complication and side-effect rates are a suitable tradeoff for possibly somewhat less symptom relief and possibly a need for retreatment in the future.

The primary purpose of this technology assessment is to review the evidence comparing newer forms of surgery or minimally invasive treatments to TURP (or other standard surgical variations), in terms of efficacy, complications, side effects, and retreatment rates.

Methods

ECRI conducted a systematic review of the controlled trial literature on surgical alternatives to standard surgeries for BPH, as well as minimally invasive treatments. These treatments were compared to either the standard surgeries (TURP, open prostatectomy, TUIP, TUEVP, TUVRP), medical therapy, sham, placebo, or no

treatment. We searched 17 electronic databases (including Medline and Embase) for relevant articles. These searches were designed to locate all controlled trials of the treatments of interest published since 1975. Searches were conducted in November 2002, and updated in January and May 2003. We also examined the bibliographies of relevant publications. These searches yielded a total of 1,811 citations. Articles that appeared to report on relevant controlled trials (as judged from their abstracts) were retrieved. These articles were read and selected by a priori standards of relevance and quality. This provided an evidence base of 145 articles reporting on 104 separate studies. Trial information and all results at all time points, including figures, were extracted and compiled in evidence tables (Volume II).

From the Evidence Tables, we conducted a systematic, qualitative, best-evidence review, giving greater value to data from studies of larger size, longer followup, and higher quality. While all results were tabled and examined, we emphasized patients' symptoms as measured by standardized indexes such as the International Prostate Symptom Score (IPSS), Madsen Score, and Boyarsky Score. We also placed some importance on the main objective physiological measures of maximum flow rate (Qmax) and post-void residual volume (PVR). The precise relationship of these measures to patient symptoms is incompletely understood. However, we believe these objective measures are of interest because it is possible they will correlate with long-term symptom results, which are scarce in the literature. We considered retreatment rates (typically with TURP) of major importance, because the less invasive treatments are intended to replace, or at least postpone TURP. We examined complication and side-effect rates, and called out any differences in these rates between the less invasive treatments and TURP.

Results and Conclusions

Specific conclusions:

- Standard surgical alternatives to TURP include transurethral electrovaporization techniques (TUEVP and TUVRP), open prostatectomy, and transurethral incision of the prostate (TUIP).
- Because electrovaporization involves skills and devices similar to those used in TURP, it can be considered a modification of TURP. Symptoms and peak urinary flow rates are similar after TUEVP, TUVRP and TURP. Quality of life is also similar after TUEVP and TURP. Both hospitalization time and catheterization time are shorter for TUEVP.
- There are no current direct comparisons of open prostatectomy to TURP. Open prostatectomy and TURP are now used on different patient populations. Open prostatectomy remains the preferred option for patients with very large prostates.
- TUIP is a recommended treatment for men with small prostates. TUIP and TURP provide similar symptom relief. TUIP results in lower retrograde ejaculation rates and shorter operation times, as well as shorter catheterization times and hospital stays than TURP. However, TURP results in higher peak urinary flow rates than TUIP.

- Contact laser ablation of the prostate (CLAP) and TURP resulted in similar improvements in physiological measures. CLAP and TURP provided similar symptom relief and similar quality of life improvements in most trials, but one double-blinded RCT found these outcomes to be less improved after CLAP than after TURP. CLAP results in less blood loss than TURP.
- One year after surgery, symptoms and quality of life improvements are similar after visual laser ablation of the prostate (VLAP) and TURP. VLAP requires shorter hospitalizations and longer catheterization times than TURP. Two trials report that major adverse events are less likely after VLAP than after TURP. Three trials report that patients who receive VLAP are more likely to require retreatment than patients who receive TURP.
- One controlled trial reported that symptoms and physiological measures improve to a similar degree after holmium laser ablation of the prostate (HoLAP) and TURP. This RCT also reported that HoLAP operations take longer than TURP operations.
- One trial reported that holmium laser resection of the prostate (HoLRP) and TURP improve symptoms to a similar degree and that HoLRP operations take longer than TURP operations, but require shorter lengths of stay and catheterization times than TURP.
- Two trials reported that after six months, holmium laser enucleation of the prostate (HoLEP) and open prostatectomy yield similar symptom improvement in patients with large prostates. Two trials reported that HoLEP required shorter hospital stays and one trial reported that HoLEP required shorter catheterization times.
- Interstitial laser coagulation (ILC) and TURP generally provide similar improvements in symptoms and quality of life. Results for physiological measures were mixed. Two trials reported higher retreatment rates after ILC. Unlike TURP, ILC may not require any hospitalization time, but this may be offset by a longer catheterization time.
- Hybrid laser techniques are too varied to permit general conclusions about this category of treatment for BPH.
- Radiofrequency needle ablation (RFNA) results in less symptom and physiological improvement than TURP up to 24 months after treatment, and two trials reported that the two treatments have similar effects on quality of life. One trial reported that decreased ejaculate and retrograde ejaculation occur less often after RFNA than after TURP.
- Only one study examined high frequency ultrasound (HIFU), but it was not randomized, and patients in its groups were not comparable.
- Cooling transurethral microwave thermotherapy (TUMT) leads to improved symptoms and physiological measures up to 12 months after treatment. Most trials report that cooling TUMT provides less symptom relief and less improvement in physiological measures than does TURP. One trial reported that retrograde ejaculation was less common after TUMT than after TURP. Retreatment rates may be higher after cooling TUMT than after TURP.

- One RCT reported that non-cooling TUMT may improve symptoms but has associated adverse events. One RCT reported that non-cooling TUMT and TURP yield similar improvements in symptoms and physiological measures, and each has different adverse events.
- One retrospective study reported that fixed stents provide more symptom relief and greater improvements in peak urinary flow rates than spiral stents, transurethral thermotherapy (TUT) and transrectal hyperthermia (TRH).
- TRH, TUT, balloon dilation, and transurethral ultrasound-guided laser-induced prostatectomy (TULIP) are outdated technologies not currently recommended by any professional organization.
- Ethanol ablation, photoselective vaporization of the prostate (PVP) and water-induced thermotherapy (WIT) are emerging therapies not yet studied in controlled trials.

General conclusions:

The purpose of newer treatments for BPH is to approximate the efficacy of TURP and the other standard surgeries while decreasing the potential harms associated with these surgeries. Some of the less invasive treatments do appear to have fewer and/or less severe immediate complications and side effects, and symptom relief approaches that of TURP. Retreatment rates suggest that symptom relief may not be as long lasting as with TURP. However, the published controlled trials are mostly small and short-term, and few of them completely reported retreatment rates (particularly the need for TURP), adverse events, and harms. Long-term effects of these treatments are currently unknown.

Introduction

Purpose of Report

The aim of this report is to provide CMS with an overview of surgical and minimally invasive procedures for the treatment of benign prostatic hyperplasia (BPH). Medical therapy is not considered in this report, except when it served as a control group. The specific purposes of this report are to:

- Review the relevant health outcomes for surgical and minimally invasive treatments for benign prostatic hyperplasia (BPH)
- Review the literature on patient utilities for outcomes of treatments for BPH
- Describe the surgical and non-surgical options for the treatment of BPH, including a narrative review of technical issues associated with each option, potential adverse effects and training issues
- Conduct a systematic narrative review of the clinical literature comparing the alternative surgical and less invasive treatment options to transurethral resection of the prostate (TURP), and to each other where possible, with attention to data on beneficial and adverse effects.

Background

Benign prostatic hyperplasia (BPH) is a condition primarily of middle-aged and elderly men. Frequency of the condition increases with age, and it is found in the majority of very elderly men. Consequently, surgical and medical treatments for BPH are some of the most common therapies administered in all of medical practice.(1,2)

BPH is a complicated condition. It can be associated with bothersome lower urinary tract symptoms (LUTS) that affect quality of life and sleeping patterns. LUTS, which may include urgency to urinate, frequent urination, weak stream, straining, and/or the sensation of incomplete bladder emptying, are usually the chief complaints of patients with BPH.(3) In the most severe stage of BPH, the inability to completely empty the bladder may progress to complete urinary blockage, which can in turn lead to kidney damage.(4)

LUTS may be also accompanied by bladder outlet obstruction (BOO), and these conditions may be caused by histologically-confirmed BPH, an enlarged prostate gland, or other causes. The Fifth International Consultation on BPH of 2001 (ICBPH) recommended that the general term LUTS be used until there is more knowledge of the causative association of BPH with particular symptoms.(5) However, only a few recent trials have followed this recommendation. Most trials used the term BPH as a general term encompassing all of the above terms, and many of the trial publications did not offer very specific definitions of BPH. Therefore, throughout this document, we use BPH as a general term for all of the above concepts.

In recent years, surgical treatment of BPH has been increasingly replaced with medical management, which can improve mild to moderate symptoms and slow the progression toward severe symptoms. However, medication may have undesirable side-effects, and may not provide adequate relief for chronic severe BPH. In such cases, surgery or minimally invasive procedures may be offered.

Transurethral resection of the prostate (TURP) is the standard surgical treatment for chronic severe BPH, although open prostatectomy may be required for men with very large prostates.(4) Transurethral electrovaporization of the prostate (TUEVP) is a procedure related to TURP that uses much of the same equipment and skills, and has come to be considered by some a standard variation of TURP. Likewise, transurethral incision of the prostate (TUIP), a less radical procedure that slices through prostate tissue rather than removing it, has also come to be considered by some a surgical standard, but limited to men with small prostates.(6)

These standard surgical procedures, however, can result in blood loss requiring transfusion, reaction to irrigation fluids (TURP syndrome),(7-11) incontinence, impotence, cardio-pulmonary events, stroke, and even death.(2,12-16) These procedures also involve regional or general anesthesia, with their inherent potential complications, a hospital stay of 1.5 days or more, as well as catheterization during one or two days of recovery. In recent years, less invasive alternatives have been explored that will minimize or altogether avoid these undesirable results.(17) Therefore, the major purpose of this report is to compare these newer less invasive technologies to TURP and its variants.

Prostate cancer detection

There can occasionally be an overlap of symptoms between prostate cancer and BPH; therefore, prostate cancer is typically investigated in the diagnostic workup of LUTS and BOO. TURP is not a diagnostic test for prostate cancer, but one advantage that it does provide while treating LUTS is that it provides tissue for histological detection of prostate cancer. This leads to early detection of some incidental cases of prostate cancer, as well as some clinically irrelevant cases. With the advent of less invasive devices and procedures for LUTS treatment that do not provide prostate tissue samples, there was concern that some incidental cases of prostate cancer could go undetected. Prostate cancer detection currently relies primarily on prostatic specific antigen (PSA) and transperineal prostate biopsies, which to some extent has allayed such concerns. Nevertheless, pretreatment PSA assays and biopsies may miss some prostate cancers that are detected at TURP.(18)

The importance of this prostate cancer detection issue and whether, or to what extent, it should influence the choice of treatment for BPH is unclear. However, the Fifth ICBPH advised that this issue be considered in men with more than ten years' life expectancy when choosing a treatment for BPH.(19) Importantly, such younger men are often considered for less invasive treatments with potentially fewer sexual side effects; and many such procedures retain no tissue for biopsy sampling. Resolution of this prostate cancer diagnostic issue is beyond the scope of this technology assessment, nevertheless, where appropriate, we mention the availability of prostate tissue samples in our descriptions of the various surgeries and less invasive treatments for BPH.

Outcome measures

Several different types of outcome measures are important when evaluating BPH treatment efficacy, and we discuss each of them when considering each treatment. Table 1 below outlines these different categories of outcome measures and provides examples of each.

Table 1. Description of Outcome Measures

Outcome measure category	Description	Examples
Symptoms	Patient's subjective experience of having BPH. Obtained using questionnaires completed by patients.	International Prostate Symptom Score (IPSS)(20) Madsen-Iverson Scale(21)
Quality of life	Patient's ability to perform daily functions and enjoy life, including cognitive abilities, activities of daily living, and family relationships. Questionnaires may relate specifically to BPH or be more generalized.	Short Form 36 (SF-36) BPH Impact Index IPSS QoL Score
Physiological measures	Patient's physiological status as it relates to BPH, including measures of prostate size and urine flow. Does not reflect patient experience.	Peak flow rate (Qmax) Post-void residual urine volume (PVR) Voided volume
Retreatment rate	Proportion of patients requiring or requesting another treatment after undergoing the treatment in question. Usually calculated a number of weeks or months after treatment.	
Adverse events	Harmful outcomes experienced after treatment, primarily physiological.	TURP Syndrome Retrograde Ejaculation
Perioperative outcomes	Outcomes that occur during or shortly after the treatment.	Procedure time Blood loss Hospitalization time

Further discussion of these outcome measures, including a discussion of advantages and disadvantages of each, is provided in Appendix A.

Patients do not view the outcomes listed in Table 1 as equally important, and different patients may perceive any single outcome differently. For example, one patient might quite negatively perceive having to get up at night to urinate, but another might not be bothered by this symptom. The notion that different patients can have different opinions about the same outcome has sparked interest in *utility assessment* in patients with BPH. Using utilities, a patient can express his opinions about the relative values of different outcomes. The available data on BPH patients' utilities are sparse: only two low-powered studies have reported such data.(22,23) Ackerman et al. (2000)(22) found that patients perceived severe incontinence and urinary retention to be the worst among the assessed long-term outcomes. Schulz et al. (2002)(23) reported that the typical patient was willing to give up 14%-20% of his lifespan in order to relieve his BPH symptoms. Background about utilities, as well as detailed tables of published utility data, appear in Appendix B.

Methods

Literature Search

To obtain information for this technology assessment, we searched 17 electronic databases (including Medline and Embase) for relevant articles. These searches were specifically designed to locate all controlled trials of treatments for BPH published since 1975. The full list of databases and search strategies is in Appendix C. Searches were conducted in November 2002, and updated in January and May 2003. We also examined the bibliographies of relevant publications. These searches yielded a total of 1,811 citations.

Selection Criteria

We read each abstract and applied *a priori* inclusion criteria (Table 2) to determine whether to retrieve the full article. We developed these criteria in consultation with The Agency for Healthcare Research and Quality (AHRQ). If the abstract left doubt about whether the article met the inclusion criteria, it was retrieved and the determination about whether to include it was made from the full text. A total of 344 articles were retrieved from the literature searches and reference lists in other articles. To avoid double-counting of patients, we extracted only unique data from multiple publications of the same trial.

Table 2. Study inclusion criteria

Category	Inclusion Criteria
Publication date	1975 through December 2002. Treatments for BPH have changed greatly since 1975, and the results of treatments before 1975 are less relevant to patients than more recent treatments.
Publication type	Full articles. The only exception to this was the inclusion of relevant abstracts presented at the May 2003 meeting of the American Urological Association. These abstracts were not included in figures or evidence tables, and our discussion of them is restricted to the text in the relevant section of the report.
Study design	Any controlled trial with at least 10 patients per group. We included controlled trials even if they were nonrandomized, historically controlled, matched controlled, retrospective controlled, or any other type of reasonably-matched comparative design. Single group studies were not included because of the known placebo and regression effects of treatments for BPH (see discussion in the earlier section on descriptions of outcomes).
Participants	Men with symptomatic BPH.
Treatments	Any treatments for men with BPH that have been published in controlled or comparative studies. This includes all of the treatments discussed in this report. The historical surgical standard of TURP was included only if it served as a control for one of the other treatments of interest.
Control treatments	Standard surgeries such as TURP, TUEVP, open prostatectomy and TUIP, as well as placebo, sham surgery, medication, watchful waiting, or no treatment. Studies of the historical standards of watchful waiting and medication were included only if they served as controls for one of the other treatments of interest.
Outcomes	We set no restrictions regarding the reporting of outcomes, because all outcomes were considered relevant.

Evidence Base

Applying the study selection criteria yielded 164 articles. We excluded 19 of these articles for reasons listed in Appendix D. Thus, the evidence base consisted of 145 articles reporting on 104 separate studies.

Data Extraction

Three methodologists extracted information from the included trials. This information included not only outcome results, but also study location, randomization, whether a trial was prospective, blinding of patients, blinding of raters, intention-to-treat analysis, and patient inclusion criteria.

Based on the recommendations of AHRQ, we extracted all reported measures at all reported time points after surgery. This allowed us to identify trends in data, and to

empirically determine whether data at earlier time points indexed treatment success as reliably as data gathered at later times. If data were reported in figures but not in text, ECRI estimated them from the figures. When study authors did not report dichotomous data as percentages, ECRI computed percentages. All extracted information, including author errors and reporting discrepancies within and between publications, is noted in the Evidence Tables.

Two additional methodologists audited all of the information entered into evidence tables from 51 of the 104 studies (49%). These 51 studies were randomly selected using a SAS random number generator. The error rate was less than 0.5%. These errors were subsequently corrected, so the total error rate, including data entry and typographical errors, in the final evidence tables is less than 0.25%.

The evidence tables for all studies and all outcomes are found in Volume II of this report. Definitions of treatment acronyms, as well as definitions of abbreviations that are in the Evidence tables, appear in Appendix E.

Analytic Approach

This report takes the form of a systematic narrative review. Evidence tables (Volume II of this report) provide an essential tool for distilling and organizing the most important information from the published clinical trials. From these tables, ECRI identified the most clinically relevant trials, organized the discussion of the results, and formulated conclusions.

Inasmuch as there were many studies of similar quality for some technologies, it was not always possible to select the "best" study for discussion and analysis. Therefore, ECRI considered the results across all relevant controlled studies wherever appropriate, giving greater weight to studies of larger size, longer followup, and higher quality.

There is not space herein to provide the numbers and full reasoning behind all of the conclusions, and the reader is directed to the evidence tables on which all of the conclusions were based.

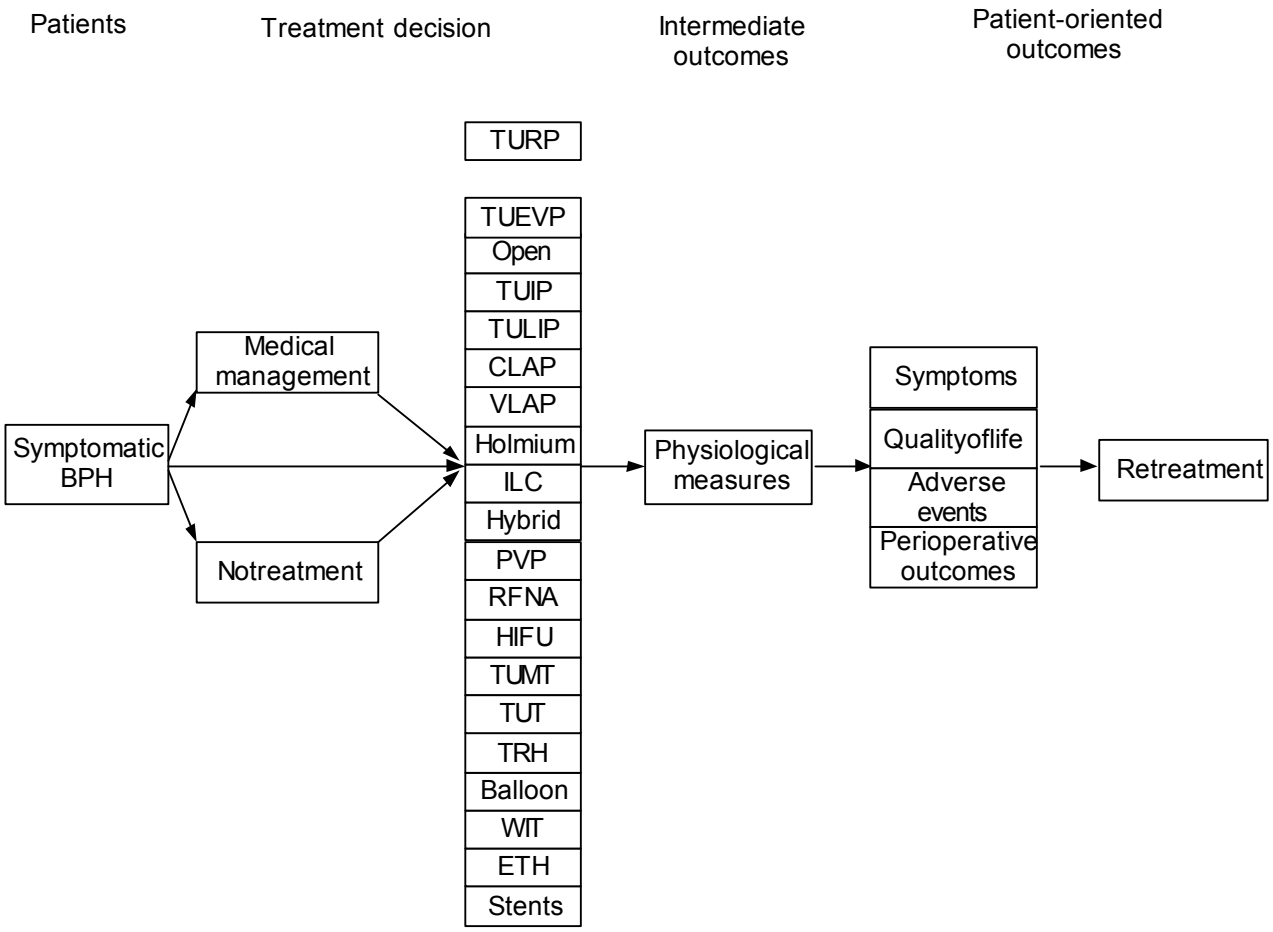
Figure 1 shows the analytic framework for this report. Patients with symptomatic BPH may have mild symptoms and thus may receive no treatment or medical management. Patients with moderate or severe symptoms that cannot be controlled through medical management may receive one of the many alternative treatments that are the focus of this report. The choice among these alternatives can be influenced by many factors including prostate size, availability of treatments at the treating institution, expertise of treating physician, and patient preference. TURP is considered the "gold standard" treatment for BPH, but less invasive treatment alternatives may be attempted first to avoid or postpone TURP (as discussed in the Introduction section).

Among the outcomes measured after treatment, some are intermediate outcomes (physiological measures of urinary tract function such as peak urinary flow rate), whereas

others are patient-oriented (symptoms, quality of life, adverse events, perioperative measures, and retreatment)[1]. The patient-oriented outcomes are more important than the intermediate outcomes because they more directly measure what matters to patients. Also, the relationship of the physiological measures to the symptoms is complex and poorly understood. Retreatment is a key outcome because it is a marker for treatment failure, and because a major rationale for the less invasive treatments is to avoid TURP. Alternatives to TURP may be associated with fewer adverse and perioperative events, but patients who receive them may be more likely to require retreatment due to insufficient resolution of symptoms. Therefore, the decision to use a new treatment may involve deciding if the tradeoff between adverse effects and efficacy is acceptable, rather than a simple decision on whether the treatment has equal efficacy with TURP. For each treatment in the Results section, we considered all of the above types of outcomes.

[1] All outcome categories are further described in Table 1 of the Introduction and in Appendix A.

Figure 1. Analytic Framework



Results

Quality of the BPH Literature

We considered only controlled trials for this evidence report, because controlled trials provide an essential context for evaluating a new treatment. A properly blinded, randomized controlled trial (RCT) provides an additional benefit of minimizing the effects of extraneous variables, so that results can be attributed solely to the treatment being studied.

Use of a control group is particularly important in studies of BPH treatment. This is because men may enter studies when their symptoms are at their worst and, these symptoms will often improve even in the absence of treatment (a phenomenon known as "regression to the mean"). We comment on data demonstrating this phenomenon in the Results section. Sech et al.(24) have also documented the existence of regression to the mean in studies of BPH.

Most of the BPH studies included in this review randomly assigned patients to groups. Randomization obviates the need to match groups on patient characteristics and baseline disease severity, although these items are presented in the Evidence Tables. Also included are a few trials that were nonrandomized prospective or retrospective comparisons that appeared to have reasonably well-matched groups of patients. A few trials that assigned treatment on the basis of prostate size or other patient characteristics were considered to have non-comparable treatment groups, and were excluded.

Almost no trials reported whether patients were blinded to their treatment, and very few studies reported blinding of outcome raters. Such reporting of blinding was so rare that we did not comment on the lack of blinding with every comparison (although it is tabulated in the evidence tables), but rather pointed out the few trials where blinding was reported. Because of the strong potential for placebo effects in BPH symptom reporting, the lack of reporting of blinding may be a cause of bias in symptom results. That is, patients who knew they received the "new" treatment may have anticipated better results and may have had a substantially stronger placebo effect than patients who knew they received the control or standard treatment. Placebo effects in objective physiological measures such as Qmax are less of a concern.

The need for equivalency trials

Medical statisticians(25-27) as well as regulatory agencies(28-33) have in recent years recognized that using trials to show that two treatments are equivalent (called "equivalency," "non-inferiority," or "active-control" trials) requires a clear *a priori* decision about the size of a clinically meaningful difference, a certain minimum study size, and appropriate statistical analysis (the null hypothesis must be reversed). Yet none of the relevant BPH trials were conducted or analyzed as equivalency trials. Using standard statistical tests designed to detect a "statistically significant difference" (typically with a p-value of 0.05) can be misleading in the absence of calculations

demonstrating adequate statistical power. Yet most of the included BPH trials did not demonstrate adequate statistical power.

Because of these considerations, many of the studies that compare BPH treatments must be cautiously interpreted. Many of them are low-powered. If a study is too small to detect a clinically meaningful difference, the finding of "no statistically significant difference" can be misinterpreted as implying equivalence.(25,34-37) Further, the less statistical power a trial has, the easier it is to misinterpret its results. Smaller trials have less statistical power to detect clinically important differences with standard statistical significance thresholds (e.g., p-values of less that 0.05). Because of the danger of such misinterpretation, and because none of the BPH trials evaluated in this report were designed and analyzed as equivalency trials by their authors, we emphasize throughout this report that "no statistically significant difference" merely means the trial cannot conclusively demonstrate a difference, and does not imply equivalence. We caution the reader against misinterpretation of such findings.

Confounds of high attrition and retreatment rates

Commonly, there were large discrepancies between the number of patients enrolled or treated and the number of patients in the results for the longest followup time. In most studies this did not appear to result from attrition, but rather because results were published before all patients had reached the longest time point ("right censoring"). While in many studies this caused the results at the longest time to be less reliable, nevertheless, this practice provided valuable information on the much-needed results at the longer time points. In general, the results at these longer time points did not appear to differ from similar time points in studies that waited for complete followup before publishing. Therefore, this large apparent discrepancy in some studies may not be a serious cause of bias.

Few, if any, of the included BPH trials were conducted strictly according to intention-to-treat principles. Few reported on patient exclusions that occurred after enrollment and before treatment, and those that did report this had negligibly small numbers of patients removed from trials in this manner. Therefore, this type of violation of intent-to-treat principles appears to be a negligible threat to validity. Patients who received a treatment almost always appeared to be kept with that treatment group for the reporting of results, even if they were subsequently treated with another treatment. Thus, in the important sense of having no crossovers, most of these studies conformed to intention-to-treat (the few exceptions are noted in the text and tables, if the authors provided such information).

In studies with high retreatment rates, interpretation of the results is difficult. In the case of dichotomous outcomes such as success/failure, retreatment could simply be counted as a treatment failure. However, there is no uniform definition of treatment failure, and few studies reported this outcome. Furthermore, recalculation and correction of reported results was beyond the scope of this technology assessment. For data that is not dichotomous, but is reported as means of continuous outcomes, there is no simple, reliable method for recalculating to account for high retreatment rates (say over about 10%). There are three possible ways authors might handle this difficulty, and they all may lead to an overestimation of the efficacy of an intervention with a high retreatment

rate. If the authors excluded the retreated patients, then the remaining patients were the patients with the best response to treatment. If the retreated patients were included as part of the analysis of results of the initial treatment, then the results not only reflect the efficacy of that treatment, but also the retreatment method, possibly inflating estimates of efficacy. If the authors crossed over the retreated cases to the arm for the retreatment method, that would be a violation of intention-to-treat principles and a threat to the original randomization. Because of these problems, retreatment rates were important to consider in arriving at our conclusions, and we treated with caution those trials that reported a high retreatment rate. In such trials, the retreatment rate itself might be the most important and only interpretable outcome.

Adverse events

In the present literature, treatment-related adverse events are incompletely reported, or are reported using different terminology and definitions. Further, many studies were too small to detect adverse events or to provide reliable rates of occurrence. If the authors did not report an adverse event, one cannot determine whether the event did not occur or if it was simply not reported. These difficulties prevented a quantitative evaluation of adverse events in this report. In the evidence tables, we included all reported adverse events as described by authors, and considered them in assessing results.

FDA Product Labeling

In evaluating the literature, it is important to determine if a given trial is applying the treatment to the population that was studied when the device received FDA marketing approval or clearance. Treatments may not be as effective for patients for whom the device or treatment was not designed. For example, treating patients with large prostates with certain laser or other heat-based treatments may not be as effective as with patients with smaller prostates for whom the treatment was intended.

Where appropriate, we mention FDA clearance indications and contraindications in the text. Full product labeling indications and contraindications for devices are provided in Appendix F. Such information was not available for all devices because many devices cleared under 510k regulations are cleared for general uses (such as many of the lasers).

Standard Surgical Treatments

Transurethral resection of the prostate (TURP)

Technology Description and Clinical Issues

TURP is considered the current standard of care for surgical treatment of BPH in most patients and has been the primary choice of treatment for the past 50 years.(3,6,19,38,39) TURP is an endoscopic procedure that requires general or spinal anesthesia and takes 30 to 60 minutes to perform. In TURP, the surgeon inserts a resectoscope, a 12-inch long, ½ inch diameter scope that contains a light, irrigating fluid valves, and a wire-loop electrode (approximately 0.3 millimeter in diameter) for cutting and coagulating. An electrosurgical generator is used to power the electrode, usually to 120 W or 150 W. The surgeon uses the wire-loop electrode to remove tissue that is obstructing or pressing

against the urethra. Prostatic tissue is generally removed until the capsule is reached. Irrigating fluid maintains the surgeon's visibility and carries the resected pieces of tissue (chips) into the bladder, which is then flushed out at the end of the TURP procedure. Higher electrosurgical frequencies may be used for coagulation during TURP. Recently, European urologists introduced a high-frequency technique called "coagulating intermittent cutting" that is intended to reduce perioperative blood loss in patients at increased risk for bleeding.(40)

Until recently, TURP procedures were performed using monopolar electrosurgery, in which an active electrode is located in the surgical handpiece, and a dispersive (return) electrode is placed on the patient (usually on the outer thigh or lower abdomen). The dispersive electrode, also called a grounding pad, directs electrical current flow from the patient back to the power unit and reduces current density as energy flows from the patient, thereby minimizing the possibility of burns at the return electrode. In bipolar TURP, much of the instrumentation and surgical technique are the same as for monopolar TURP. A dedicated bipolar electrosurgical generator may be used, but some general electrosurgical devices can be used for both modes. Also, both modes can be used in the same procedure, for example, for cutting and coagulating. Dual wire-loop electrodes are used, in which the active and return electrodes are located in one handpiece, and the electrosurgical current flows between the electrodes through conducting saline, rather than from the active wire-loop electrode, through the patient to the grounding pad (dispersive electrode) as in monopolar TURP. Therefore, the dispersive electrode pad placed on the patient is not required in bipolar TURP. Because of the differences in energy delivery, bipolar TURP can result in less granulation tissue and less tissue charring than monopolar TURP. However, bipolar TURP requires slower movement of the wire-loop electrodes. Bipolar electrodes require less power than monopolar electrodes, because there is less tissue between the electrodes to create impedance.(41)

Monopolar TURP requires the use of a nonconducting irrigation fluid. Sterile water was used up until the 1940s, when it was abandoned because of problems with hemolysis.(42) The current standard irrigant is 1.5% glycine, although mannitol and sorbitol have also been used.(42) Absorption of excess irrigation fluid into the blood stream can cause TURP syndrome, which can include hyponatremia, nausea, temporary blindness, unconsciousness, and rarely death.(7) Bipolar TURP requires saline for current conduction between the two electrodes. This has the potential to eliminate TURP syndrome. However, the use of saline in the narrow urethra introduces the potential for inadvertent damage to non-targeted tissue.

Our searches identified no controlled studies directly comparing mono- and bipolar techniques. Only one of the trials included in the present analysis reported which method was used (monopolar),(43) possibly because both methods are considered versions of the standard TURP procedure. Therefore, there is insufficient evidence to draw conclusions about the comparative effects of these two techniques on patient outcomes.(8-11)

It is considered undesirable to have a TURP procedure last longer than 60 minutes, because of potential blood loss and irrigation fluid absorption. This has the practical

effect of preventing the use of TURP for patients with very large prostates beyond the 70 to 100 grams range,(19,44) and such patients may require open prostatectomy.

TURP requires catheterization for 24 to 48 hours, and a hospital stay ranging from one to five days. In addition, for at least four weeks after TURP, patients may have restricted physical activity.

In a recent landmark study by Borboroglu and colleagues of 520 consecutive TURP patients from 1991-1998,(45) the rate of intraoperative complications was 2.5%, immediate postoperative 10.8%, and late complications 8.5%. The transfusion rate was 0.4%. There were no mortalities, meaning the rate was less than 0.2% (1/520). The rate of repeat TURP was 2.5%, with mean followup of 42 months (range: 6 to 84 mos.). These authors found great improvements in all the above rates compared to compilations from previous eras that have often been used by proponents of new treatments in retrospective comparisons to historical controls. In the first year of the Borboroglu study (1991), the catheterization time was 3.5 days and hospital stay 3.8 days, but these were reduced to 1.8 and 1.1 days, respectively, for the last year of the study (1998). These large improvements in results over time suggest that even the rates cited in this most recent study may overestimate the TURP complication rates observed in current practice. This indicates the unreliability of comparing uncontrolled study results to historical data. Thus, we base our report mostly on controlled studies in which new treatments were compared directly to a concurrent TURP group.

In 21 controlled trials included in the present report with TURP groups with followup of at least 12 months, the retreatment rate in the TURP groups ranged from 0% (0/35)(43) to 30% (13/43)[2].(46) However, the definitions of "retreatment" in these trials were not consistent. Trials with smaller retreatment rates appeared to refer only to TURP retreatment for LUTS, whereas, trials with larger rates appeared to refer to any urological surgical intervention for any reason during followup. Because of the lack of a consistent definition, as well as other between-study differences, across-studies comparisons of retreatment rates are inappropriate in this body of evidence, and the reader is advised to consider only the within-studies comparisons of retreatment rates. Because of the small size of many of the studies and the low frequency of retreatment, even the within-studies retreatment rate comparisons may not be reliable.

TURP is performed with general surgical devices such as electrosurgical units, electrodes and endoscopes. These devices are cleared for marketing in the United States through the Food and Drug Administration's 510(k) premarket notification process.(47)

Clinical Practice Guidelines

In 2000-2001, the Fifth International Consultation on BPH (ICBPH), sponsored by the World Health Organization (WHO) and the Union Internationale Contre le Cancer (UICC), established recommendations for the diagnosis and treatment of BPH, lower

[2] Adverse event and reoperation rates are always provided with raw numbers as well in this document, unless the authors did not report the number of patients that the statistic was based on.

urinary tract symptoms, and bladder outlet obstruction.(48) Recommendations were based on a literature review and opinion of international clinical experts. The Fifth ICBPH considers TURP the "gold standard of interventional therapy" for BPH,(5,19) but suggests that, because morbidity, mortality, and blood transfusion rates are directly related to resection time, TURP should only be performed if the resection can be completed in one hour.(19) The European Association of Urology (EAU) recommends surgical management using TURP, TUIP, or open prostatectomy as a first-line treatment for patients with bothersome BPH symptoms refractory to medical treatment.(49) The AUA also considers TURP to be "the gold standard" for BPH treatment.(3)

As TURP is the current standard of care, it is outside the scope of this report to provide a detailed analysis of its efficacy. The above comments are provided as background information.

Transurethral electrovaporization procedures

Technology Description and Clinical Issues

Transurethral electrovaporization of the prostate (TUEVP, TUVAP, or TUEVAP; also called transurethral vaporization, TUVP or TVP, or transurethral evaporation, TUEP) has developed since the early 1990s as a variation of TURP. TUEVP and TURP are similarly performed in that both use a standard resectoscope inserted transurethrally, and an electrosurgical unit to deliver energy to an electrode. Thus, TUEVP is considered a modification of TURP.(19,50-52)

Electrovaporization procedures differ from TURP and each other according to the type of electrode used and the magnitude of electrical energy applied, both of which determine whether tissue is incised, vaporized, resected into pieces or "chips", or coagulated. In general, the electrodes used in vaporization procedures are shaped and sized to allow more tissue contact than the standard thin wire loop electrode used for resecting. Prostatic tissue is vaporized using a grooved or spiked rollerball or thicker band-loop electrode. Wire loop electrodes used for electrovaporization are approximately one millimeter in diameter. Due to the high energy and simultaneous vaporization/coagulation of prostate tissue, TUEVP procedures can produce less bleeding than TURP.(19,53,54) After the electrode is inserted through the resectoscope to the area to be treated, an electrical current of 230 to 300 W is applied to heat the obstructing prostate tissue until it turns to steam. A constant flow of irrigating fluid is applied to the heated area to dissipate heat. According to clinicians, TUEVP is difficult to perform in prostates larger than about 50 grams, because of the longer operative times required.(55)

"Sandwich techniques" have been developed that use the rollerball electrode to vaporize and coagulate first, followed by the standard TURP wire-loop electrode to resect coagulated tissue, and then the rollerball electrode again to complete dissection and coagulation of deeper tissue. In this report, we refer to any technique combining vaporization and resection as transurethral vaporization with resection of the prostate (TUVRP). The "sandwich technique" allows tissue to be removed for pathologic analysis.(53) In addition to the sandwich technique, TUVRP can also be performed with a single thicker loop or band electrode. This enables more contact with prostate tissue

than the TURP thin wire-loop electrode, to simultaneously vaporize, cut, and coagulate, without alternating the electrode used. For cutting, energy of 230 to 300 W is used, and for coagulation, energy of 50 to 80 W is used. Regardless of the power setting, the actual power delivered depends on the impedance of the tissue. Too low power can result in less efficient cutting and excess coagulation necrosis, which is considered a cause of persistent postoperative irritative symptoms.(53) Some power generators have the ability to increase current with changing tissue impedance. With TUVRP, resection of tissue "chips" is possible, although cutting times are longer than with TURP because of the time required for vaporization and coagulation. In 2002, a bipolar electrosurgical generator for plasma vaporization and resection was introduced and is being studied in comparison to TURP and TUVRP.

Electrovaporization procedures can be performed on an outpatient basis or with an overnight hospital stay. Depending on the patient, general or regional anesthesia, and/or intravenous sedation with local intraurethral analgesic are used. Theoretically, vaporization causes less bleeding because the treated tissue is coagulated and sealed by the higher applied energy and the electrode design (the evidence for this is addressed below). TUEVP and TUVRP are considered easy to teach and learn, because of the similarity to TURP in equipment and technique, and the better visibility due to less bleeding.(52)

In our analysis comparing TUEVP with TURP, we considered all TUEVP procedures as a group and did not separate results based on the many different electrode designs. This is in accordance with the way the procedure is commonly categorized by clinicians in the literature. We considered TUVRP to be a separate technique and analyzed these trials separately.(55)

TUEVP and TUVRP are performed with general surgical devices such as electrosurgical units, electrodes and endoscopes. There are many electrodes with different shapes for TURP, TUEVP and TUVRP. The electrodes used in the included trials in the present report are listed in the evidence tables that accompany this report. These devices are cleared for marketing in the United States through the Food and Drug Administration's 510(k) premarket notification process.(47)

Clinical Practice Guidelines

The Fifth ICBPH views TUEVP as a variation of the standard TURP procedure that results in less bleeding, and has considered TUVRP an "acceptable" BPH treatment since 1997.(19) The AUA concluded(56) that TUEVP shows equivalent short-term symptom improvement to TURP, but has higher rates of postoperative irritative urinary side effects. The AUA states that long-term comparative trials are needed to compare transurethral vaporization to standard TURP. In addition, the AUA considers the newer bipolar plasma vaporization technique an emerging therapy requiring additional data before it can be recommended as a treatment option. The procedure can be offered to appropriate patients, provided outcomes relative to recommended treatments are discussed with the patient.(3)

Findings

- **Symptoms and peak urinary flow rates are similar after TUEVP, TUVRP and TURP. Quality of life is also similar after TUEVP and TURP. Both hospitalization time and catheterization time are shorter for TUEVP.**

Seventeen controlled trials compared TUEVP or TUVRP with TURP (N ≥1,100), all but one of which were randomized.(44,50-52,55,57-70) Most studies that reported size criteria excluded patients if their prostates were over 60 or 70 grams. Most trials had data at one year, one trial at two years and one at three years. Thirteen trials evaluated TUEVP, while four trials used a combination of cutting and vaporization (TUVRP).(55,57,58,66)

TUEVP

Twelve trials on TUEVP reported symptom severity. In general, after TUEVP and TURP, patients' symptoms improved from severe to mild, and patients' IPSS scores were similar. TUEVP and TURP also provided similar peak urinary flow rates (Qmax; reported by 15 trials). Five(50,57,60,61,63,71) of the 13 trials on TUEVP reported quality of life (QoL) data, and, again, similar results were observed after the two treatments.

The number of patients with retention, stricture, incontinence or retrograde ejaculation was similar after TURP and TUEVP. Five studies reported on post-operative irritative symptoms (caused by sloughing of necrotic tissue). Four of these trials reported more such symptoms with TUEVP than with TURP.(50,60,67,69) However, in one trial, the rates were similar.(61)

Two trials reported retreatment rates.(63,68) These rates tended to be lower after TURP but rates were so low for both groups that reliable comparisons cannot be made.

Results for operation time wee mixed: operation time was shorter for TUEVP in two trials,(51,65) shorter for TURP in two(50,61,70) and the same in two.(60,67) Catheterization time was shorter for TUEVP in seven of eight trials reporting.(50,51,61,65,67,68,70) Hospital stay was shorter for TUEVP in four of five trials reporting this result.(50,61,68,70)

TUVRP

Four trials evaluated TUVRP(55,57,58,66) and found that results were similar for TUVRP and TURP for symptoms and physiological outcomes. Across trials TUVRP and TUEVP showed similar results for symptoms and physiological outcomes, although there was no such direct comparison in any trial.

Operation time was longer for TUVRP in two trials(55,58) and the same in two.(57,66) Catheter time was shorter for TUVRP in one trial (48 hrs, vs 96 hrs,)(58) and the same in one (3.4 and 3.3 days).(66) Hospital stay was shorter for TUVRP in the only trial reporting this result (2.5 days vs 4.5 days).(58)

Open prostatectomy

Technology Description and Clinical Issues

Open prostatectomy is a major surgical procedure in which the obstructing prostate tissue is removed through a lower abdominal incision using a suprapubic (through the bladder) or retropubic (through the prostate capsule) approach. The obstructing tissue is excised in one piece, and the prostate capsule is not removed. (In radical prostatectomy, a treatment for prostate cancer, the entire prostate and capsule are removed.) Open prostatectomy requires general or spinal anesthesia, a three- to five-day hospital stay, and a longer period of catheterization and recovery than TURP. Open prostatectomy is one of the only treatment options for patients with prostate glands greater than 75 to 100 grams,(19,44) and is also performed in patients with other conditions, such as bladder stones, that require an open procedure.(19,49) Therefore, today TURP and open prostatectomy are considered for different populations of patients, and are not considered to directly compete with each other.

In the past, although TURP may have been no better than open prostatectomy in terms of symptom improvements and not quite as efficacious in terms of physiological measures, these differences were considered to be outweighed by the shorter operation times and less blood loss. This accounts for TURP's historical replacement of open prostatectomy as the "gold standard" surgical treatment for BPH, except for men with very large prostates beyond the 70 to 100 grams range.

As a surgical procedure, open prostatectomy is not regulated by the FDA.

Clinical Guidelines

The Fifth ICBPH considers that open prostatectomy is "acceptable," and that it is necessary for patients with prostates larger than 80 to 100 grams. The EAU recommends surgical management using TURP, TUIP, or open prostatectomy as a first-line treatment for patients with bothersome BPH symptoms refractory to medical treatment.(49)

Findings

- **There are no current direct comparisons of open prostatectomy to TURP. Open prostatectomy and TURP are now used on different patient populations.**

There has been only one controlled trial comparing open prostatectomy with TURP, a randomized study by Meyhoff (N = 75) in the 1970s.(46,72) The efficacy and complications for these procedures at that time are likely not relevant to current practices; TURP and open prostatectomy are now considered to have different indications and patient populations.(19)

Transurethral incision of the prostate (TUIP)

Technology Description and Clinical Issues

TUIP is a surgery that is less invasive than TURP and is usually limited to small prostate glands. In TUIP, the surgeon makes one or two lengthwise internal incisions in the prostate near the bladder, which opens the bladder neck and prostate to reduce pressure

on the urethra. Either a laser system or electrical current delivered via an electrosurgical unit can be used to make the incisions (only electrosurgical incisions are considered in this section; laser surgeries are considered in other sections). Because TUIP is less invasive than TURP, it can be performed on an outpatient basis under regional or general anesthesia, although a one- to three-day hospital stay may be required. Although the incision itself does not provide prostate tissue for histological detection of prostate cancer, a biopsy can be taken through the resectoscope at the time of the procedure.(73)

TUIP is performed with general surgical devices such as electrosurgical units, electrodes and endoscopes. These devices are cleared for marketing in the United States through the Food and Drug Administration's 510(k) premarket notification process.(47) They are not generally cleared for specific indications.

Clinical Practice Guidelines

TUIP is performed on patients with small prostate glands. The World Health Organization recommends restricting the use of TUIP to patients with prostates 30 grams or less in size.(6) The European Association of Urology (EAU) recommends TUIP for patients with a small prostate gland, no median lobe, and a low risk of associated prostate cancer.(49) The Fifth ICBPH suggested that TUIP can be used to treat prostates up to 80-100 grams in size, but is particularly suited for treating prostates of less than 30 grams.(19) The EAU recommends surgical management using TURP, TUIP, or open prostatectomy as a first-line treatment for patients with bothersome BPH symptoms refractory to medical treatment.(49)

Findings

- **TUIP is intended for men with small prostates. TUIP and TURP provide similar symptom relief. TUIP results in lower retrograde ejaculation rates and shorter operation times, as well as shorter catheterization times and hospital stays than TURP. However, TURP results in higher peak urinary flow rates than TUIP.**

We identified 10 randomized trials (N = 811) comparing TUIP to TURP.(73-85) Most of these trials followed the majority of patients for two to three years. These trials included only men with prostates smaller than 20 to 40 grams. In these trials, the symptom relief for the two treatments appears similar, but peak urinary flow rate (Qmax) was higher after TURP. None of the studies reported data on quality of life.

After TUIP, operation time, days in hospital, and catheterization time were shorter or similar to TURP, and a lower or a similar percentage of patients required transfusions. While most adverse events were similar, the retrograde ejaculation rate was lower after TUIP.

Retreatment rates were reported in four trials.(74,76,77,80) In three of the four trials, retreatment rates appear higher for TUIP than for TURP. One study of 85 patients (Jahnson 1998) reported that this difference was statistically significant (23% versus 5% retreatment rates),(76) while two reported no statistical tests and one reported no statistically significant differences (exact rates not available). However, because the number of patients enrolled in each of these trials was either not reported or was often

small (<35 patients per group) and the number of patients requiring retreatment was also low (typically <10), comparison of rates may not be reliable.

The 5-year trial by Jahnson et al. (1998)(76) carried out cystoscopy at 2 years and found adhesions, closed incisions or obstructing lobes in 90% (19/21) of the TUIP patients compared to 39% (9/23) of the TURP patients (statistically significant). A comparable difference was observed at five years. These authors concluded that these findings explained why Qmax is lower and the retreatment rate is higher for TUIP.

Laser Surgical Treatments

Transurethral ultrasound-guided laser-induced prostatectomy (TULIP)

Technology Description and Clinical Issues

TULIP was introduced in 1990 and was one of the first laser procedures used for BPH. TULIP is performed with a right-angle-firing Nd:YAG laser probe housed between two ultrasound transducers that are used for real-time sector scanning to position the laser while it is being fired. The laser is fired while the device is moved and rotated through the urethra from the bladder neck to the verumontanum. Coagulation necrosis of the prostate tissue produces shrinking over several weeks following the procedure.

TULIP has been replaced by other laser types and techniques (discussed in subsequent sections) that have fewer side effects, shorter postoperative catheterization times, and fewer urinary symptoms. The most recent controlled trial of TULIP was a retrospective review published in 1998 by Japanese researchers, and the patients had likely received the procedure several years before then.(86)

Clinical Practice Guidelines

TULIP is not mentioned in any of the evidence-based BPH guidelines that we identified.

Findings

Because this treatment appears to be outdated, we do not further consider the results of controlled trials on it.

Contact laser ablation of the prostate (CLAP)

Technology Description and Clinical Issues

Surgeons developed CLAP in the early 1990s in an attempt to avoid the intraoperative complications of TURP, such as blood loss. To perform CLAP, the surgeon places the tip of an Nd:YAG laser in direct contact with the prostatic tissue, which vaporizes it. The laser tip is slowly dragged to create “furrows” across the prostate, thereby reducing prostatic obstruction of the urethra. While the primary mechanism of action in CLAP is vaporization, some tissue coagulation also occurs. As a result, patients require postoperative catheterization to permit sloughing of any coagulated tissue. Unlike TURP, CLAP does not yield samples that can be tested for prostate cancer. CLAP requires extensive training and experience, and some have suggested that a surgeon’s first set of cases be restricted to patients with smaller prostates because they are easier to treat.

Results from one RCT suggested that some surgeons experienced difficulty in performing CLAP in patients with prostates of 40-50 grams.(87) We identified a single laser FDA cleared specifically for use during the CLAP procedure: Surgical Laser Technologies' SLT CL MD (Nd:YAG) Contact Laser System and delivery fibers.(88) This laser is cleared only for prostates up to 45 grams.

Clinical Practice Guidelines

The AUA 2003 Guidelines(3) classify CLAP as a surgical approach to BPH and states that the choice of surgical approach is a technical decision based on patient's prostate size, surgeon judgment, and patient's comorbidities. The AUA also states that, while CLAP results in short-term improvements (symptom scores, urinary flow rate) equivalent to TURP, reported rates of postoperative urinary retention and unplanned secondary catheterization are higher following CLAP.

The Fifth ICBPH(19) recommends holmium laser treatment and ILC over CLAP due to CLAP's higher treatment failure rates and complications. The EAU(49) does not discuss CLAP in its review of laser therapy, but recommends that side-firing VLAP and ILC be used only for patients on anticoagulants, for patients not eligible for TURP, or for patients with a desire to maintain ejaculation.

Findings

All five of the trials comparing CLAP to TURP used sapphire-tipped laser probes and fibers (MTRL 10) manufactured by Surgical Laser Technologies (Oaks, PA, USA). Four of the five trials used an Nd:YAG laser generator manufactured by the same company,(71,89-91) and the fifth trial used an unspecified Nd:YAG laser generator.(89) There were no controlled trials comparing CLAP devices. However, the similarities among the CLAP devices in these five trials support the grouping of their results.

- **CLAP and TURP resulted in similar improvements in physiological measures. CLAP and TURP provided similar symptom relief and similar quality of life improvements in most trials, but one double-blinded RCT found these outcomes to be less improved after CLAP than after TURP. CLAP results in less blood loss than TURP.**

Five controlled trials (N = 346) compared CLAP to TURP.(71,87,89-95) These trials were all randomized, and one was a double-blinded trial that followed patients for three years (the Oxford Laser Prostate trial).(87,91-94) In that trial, symptoms were worse at three years for patients who received CLAP than for those who received TURP(statistically significant). The other four trials found that symptom scores after CLAP and TURP were similar. All five trials found that physiological measures such as Qmax were similar for CLAP and TURP after treatment.

The Oxford trial found that one year after treatment, BPH-specific quality of life was slightly worse after CLAP than after TURP (statistically significant). However, quality of life using other measures in other trials was similar after the two treatments.

Two trials reported retreatment rates.(87,89,91,94) Keoghane et al. (2000) reported that patients who received CLAP were more likely to require retreatment by three year followup than those who received TURP (18% vs 9%) (statistical significance not reported). The authors suggest that this difference may have been caused by surgeons' limited experience with CLAP.(91) Another possible explanation is the inclusion of patients with large prostates, who are more difficult to treat and may be less appropriate for CLAP. Three of the five trials(89,90,95) either excluded patients with large prostates (e.g., >40 grams) or required surgeons to have performed a minimum of 20 previous CLAP procedures.(90) One of these three trials (Tuhkanen et al., 1999)(89) reported that no patients in either group required retreatment, suggesting that it enrolled too few patients to reliably determine retreatment rates.

Operation times for CLAP and TURP were generally similar (30-40 minutes), but two trials reported that during CLAP, patients lost significantly less blood (37-59 mL versus 175-200 mL during TURP).(89,91)

Three of the five trials reported comparative data on adverse events. One trial (N = 32) found a statistically significantly lower rate of retrograde ejaculation after CLAP than after TURP (6% versus 81%).(89) None of the other trials reported retrograde ejaculation rates. No other statistically significant differences in adverse event rates were reported, but it is possible that the trials enrolled too few patients to detect such differences.

Visual laser ablation of the prostate (VLAP)

Technology Description and Clinical Issues

In VLAP,[3] the Nd:YAG laser is held a short distance (2 mm) from the prostate tissue (unlike CLAP in which there is direct tissue contact, see previous section). The primary mechanism of tissue destruction is coagulation rather than vaporization, and the coagulated tissue sloughs away over the next several weeks. Therefore, VLAP requires longer postprocedural catheterization times ranging from five days to several weeks, and may require recatheterization. During the sloughing period, patients may also experience infection, swelling, and pain during urination. Several variations of VLAP have been developed that use different types of lasers, laser fibers, wattages, and application techniques. Unlike TURP, VLAP does not yield samples that can be tested for prostate cancer.

VLAP is typically reserved for patients with small or moderately-sized prostates (<80 grams), because patients with larger prostates would require multiple sessions. Patients with chronic urinary tract infection or bacterial prostatitis are not good candidates because coagulated tissue may become infected.(19) VLAP may be particularly appropriate for patients who are on anticoagulants because the laser seals blood vessels.

VLAP devices that have received FDA 510(k) clearance to be marketed in the treatment of BPH include Trimedyne's Optilase Nd:YAG Laser System Models 1000, 4000, and

[3] VLAP is also referred to as non-contact laser ablation of the prostate or laser coagulation of the prostate.

1000-100 (PL100) used with Trimedyne's UroGold or UroMax Right Angle Laser Fibers, and Laserscope's 800 Series and Orion Series KTP/Nd:YAG Surgical Laser Systems used with the Angled Delivery Devices (ADD Family Product Line). The Trimedyne system is indicated for coagulation of soft tissue for prostatectomy in the treatment of BPH. The FDA clearance did not mention whether the device was indicated for patients with specific prostate sizes. The Laserscope system is indicated for men 50 years and older with prostatic volumes of 60 cc or less.

Clinical Practice Guidelines

The AUA Guidelines(3) classify VLAP as a surgical approach to BPH and states that the choice of surgical approach is a technical decision based on patient's prostate size, surgeon judgment, and patient's comorbidities. AUA also states that, while VLAP results in short-term improvements (symptom scores, urinary flow rate) equivalent to TURP, reported rates of postoperative irritative voiding and unplanned and prolonged postoperative catheterization are higher following VLAP.

The Fifth ICBPH(19) classifies VLAP as an "acceptable" treatment, but recommends holmium laser treatment and ILC over VLAP due to higher retreatment rates and complications. The EAU guideline(49) does not recommend VLAP as a first-line therapy, but advises that VLAP be used only for patients on anticoagulants, for patients not eligible for TURP, or for patients with a desire to maintain ejaculation.

Findings

Ten trials compared VLAP to TURP. Eight of these trials(95-102) used the Urolase fiber (Bard, Covington, GA, USA), one(103) used the Ultraline fiber (Lasersonics, Tokyo, Japan), and one(63) used the ADD fiber (Laserscope, San Jose, CA, USA). No controlled trials of VLAP have compared these fibers, thus one cannot determine from direct evidence whether the different fibers in these studies affected results. Regarding laser generators, seven(63,97-102) used an Nd:YAG laser from an unspecified manufacturer, one(103) used the Hercules 5060 Nd:YAG laser generator (Lasersonics, Tokyo, Japan), one(96) used the Trimedyne Nd:YAG laser (Trimedyne, Irvine, CA, USA), and one(95) used the SLT Nd:YAG laser (Surgical Laser Technologies, Oaks, PA, USA). As with the fiber differences, because of the lack of controlled trials comparing generators, one cannot determine whether device differences could have affected outcomes.

- **One year after surgery, symptoms and quality of life improvements are similar after VLAP and TURP. VLAP requires shorter hospitalizations and longer catheterization times than TURP. Two trials report that major adverse events are less likely after VLAP than after TURP. Three trials report that patients who receive VLAP are more likely to require retreatment than patients who receive TURP.**

Ten trials (eight of them randomized) compared VLAP to TURP.(63,64,95-108) The trials enrolled over 1,057 patients. One of these, the CLASP randomized trial, also included a group of patients who received only "conservative management," and VLAP patients fared significantly better in symptom score improvement than those patients.(100,105,109) Of eight studies reporting IPSS scores at 6-8 months of followup,

four(63,64,98,101,102) reported statistically significantly fewer symptoms after TURP than after VLAP. None of the three studies reporting twelve month or longer followup reported any statistically significant differences in IPSS scores.(63,64,95,97) Four of five studies reporting quality of life data found no statistically significant differences between VLAP and TURP.(63,64,96,100-102,104-108) Of five studies reporting peak urinary flow rates at one year or longer, two(95,96,106-108) found no significant differences between VLAP and TURP, and three(63,64,97,99) did not report statistical tests of this outcome.

Of four trials reporting operation times, one study with multiple publications(96,106-108) reported statistically significantly shorter operation times for VLAP than for TURP, one study(95) reported no statistically significant difference, and the other two studies(100,103-105) did not report statistical tests of this outcome. Of eight trials reporting hospitalization times, five(95,96,100-102,104-108) reported that it was statistically significantly shorter after VLAP than after TURP. Of eight trials reporting catheterization times, four(63,64,100-102,104,105) reported that catheterization times were statistically significantly longer after VLAP than after TURP. Of seven trials(63,64,96,97,99-101,103-108) reporting rates of blood transfusion, one study with multiple publications(96,106-108) reported statistical tests of this outcome, and it reported no statistically significant difference.

Two trials reported that significantly fewer major adverse events (e.g., urethral stricture) occurred in patients who receive VLAP than those who received TURP (8-11% VLAP versus 30-36% TURP).(96,101)

Three prospective trials reported retreatment rates,(99,101,102) and they all found that retreatment was more common after VLAP than after TURP (7-9% versus 0-4%, respectively).

- **CLAP and VLAP yield similar improvements in symptoms and peak urinary flow rates. The findings on retreatment rates are mixed.**

Three RCTs with one to two year followup compared CLAP to VLAP.(95,110,111) Both treatments reduced symptoms in all three trials to a similar degree. Peak urinary flow rate (Qmax) also improved similarly after both treatments.(95,110,111) Findings on retreatment rates, reported by two trials, were mixed; Narayan, 1995(111) found that 0/32 (0%) CLAP patients required retreatment as compared to 5/32 (16%) of TURP patients (statistically significant difference). Bryan (2000)(110) reported similar retreatment rates after CLAP and VLAP (4.8%, or 1/21 patients versus 11.8% or 2/17 patients) but may have had insufficient statistical power to detect a difference in retreatment rates.

Three trials reported catheterization time; although Bryan, 2000 found longer catheter times after VLAP (13.2 days versus 4.5 days for CLAP)(110), the other two trials did not find such differences (one to two days for both treatments).(95,111)

- **One RCT reported long-term results comparing VLAP to hybrid laser and found similar results on symptoms, peak urinary flow rates, retreatment, adverse events rates, and perioperative outcome measures for the two treatments.**

One RCT (N = 93) with three-year followup compared VLAP with Urolase fiber to a hybrid laser technique using the Ultraline fiber.(112-114) Symptoms, physiological measures, retreatment, adverse events, and perioperative measures were all similar after the two treatments.

Holmium laser treatment

Technology Description and Clinical Issues

Surgical use of the holmium laser for BPH has evolved since its original introduction in 1994. Initially, holmium laser ablation of the prostate (HoLAP) was performed and involved the use of side-firing and end-firing laser fibers to vaporize and ablate prostate tissue. Relief of obstruction is immediate, unlike other laser procedures such as VLAP in which benefits are seen only after a delay. However, HoLAP does not yield tissue for histologic analysis, therefore surgeons later developed holmium laser resection of the prostate (HoLRP).

In HoLRP, the surgeon resects prostate tissue into pieces small enough to be removed with bladder irrigation and grasping forceps or a modified resectoscope loop. Compared to TURP, however, HoLRP yields less tissue for analysis, and the available tissue is of lower quality due to thermal artifacts.(115) These problems, in addition to relatively long operation times, motivated the development of Holmium laser enucleation of the prostate (HoLEP) in conjunction with a tissue morcellator.

In HoLEP, an entire prostatic lobe can be separated from connective tissue and deposited into the bladder. The removal of intact lobes is similar to open prostatectomy, discussed above. The morcellator then extracts the tissue from the bladder without using heat, thereby preserving tissue volume and quality. Bladder injuries related to careless operation of the morcellator have been reported; distension of the bladder can prevent the bladder mucosa from being drawn into the blades.(116) In the Findings section below, the three Holmium procedures (HoLAP, HoLRP, and HoLEP) are discussed separately.

Prostate size is an essential factor in the choice of holmium laser procedures. For patients with small prostates, HoLAP may still be appropriate,(116) and incision of the bladder neck using the holmium laser is another alternative.(115) Moderately-sized prostates can be treated with HoLRP.(117) One possible advantage of HoLEP is that with sufficient surgical expertise, it can be applied to very large (>100 grams) prostates.(115)

An advantage of the holmium laser is the ability to coagulate tissue simultaneously with tissue incision, vaporization, resection, or enucleation. This reduces intraoperative blood loss as well as postoperative bleeding. However, holmium lasers are expensive, and the surgical procedures generally require extensive training.(115-117) Therefore, fewer urologists are likely to offer this treatment option to patients. A minimum of 20-30 cases

using HoLEP on small prostates may be necessary before a surgeon is sufficiently skilled to treat patients with larger prostates.(116)

Many holmium lasers have been FDA approved for general urological indications. Among them, specifically listing HoLEP, HoLAP, and HoLRP as intended uses, is the Modified Lumenis VersaPulse PowerSuite Holmium and Dual Wavelength Surgical Laser System.(FDA clearance product number K011703).(118) The system is indicated for use in a variety of urological indications including BPH, lithotripsy, and tumor removal. The FDA clearance did not mention whether the device was indicated for patients with specific prostate sizes.

Clinical Practice Guidelines

The Fifth ICBPH favors the use of the holmium laser over CLAP and VLAP, although they emphasized that there is a steep learning curve associated with holmium laser use.(19) The ICBPH guidelines also stated that prostates larger than 100 grams are a relative contraindication, but noted that the development of morcellators has improved retrieval of larger prostate fragments from the bladder. The EAU guidelines recommend laser prostatectomy using side-firing lasers or interstitial laser coagulation (ILC) for patients who are on anticoagulant medication, who are not candidates for TURP, or who desire to maintain ejaculation. The EAU noted that holmium laser resection/enucleation is a promising technique with outcomes similar to TURP.(49) The AUA considers holmium laser resection/enucleation an alternative to TURP in medical facilities that have the technology and training.(3)

Findings

Holmium Laser Ablation of the Prostate (HoLAP)

The only study available evaluating HoLAP(119) used the VersaPulse Select laser (Lumenis, Santa Clara, CA, USA). Two fibers were used: the Slimline 550 (Lumenis, Santa Clara, CA, USA) or the Duo-Tome Sidelite (Lumenis, Santa Clara, CA, USA).

- **One controlled trial reported that symptoms and physiological measures improve to a similar degree after HoLAP and TURP. This RCT also reported that HoLAP operations take longer than TURP operations.**

One RCT (N = 36) compared HoLAP to TURP (Mottet et al. (1999)(119) with one-year followup. Symptoms and physiological measures improved to a similar degree after both HoLAP and TURP. However, this is based on only 36 patients.

Mottet et al. (1999)(119) found that HoLAP operations took statistically significantly longer (mean 75 minutes) than TURP operations (mean 40 minutes), but they found no differences in other perioperative measures. Enrollment may have been too low to reliably detect differences in adverse events between HoLAP and TURP. Retreatment data beyond six months after surgery were not reported.

Holmium Laser Resection of the Prostate (HoLRP)

All three trials of HoLRP used the VersaPulse pulsed holmium laser (Lumenis, Santa Clara, CA, USA). One trial(86) used the Slimline fiber, and the other two(18,120) did not specify the fiber that was used. No published controlled trials have compared the use of different HoLRP devices. In general, however, the devices appear to be the same or similar in different studies, which supports the grouping of these HoLRP studies.

- **One trial reported that HoLRP and TURP improve symptoms to a similar degree and that HoLRP operations take longer than TURP operations. However, HoLRP requires a shorter length of stay and catheterization time than does TURP.**

One RCT (N = 120) compared HoLRP to TURP.(18,121,122) At two-year followup, improvements in symptoms after HoLRP were similar to those after TURP.

These authors also reported statistically significantly longer operation times for HoLRP (mean 41.5 minutes) than for TURP (25.3 minutes). However, patients who received HoLRP experienced statistically significantly shorter hospital stays (mean 1.1 days vs. 2.0 days) and catheterization times (0.8 days vs. 1.6 days) than patients who received TURP. The study also reported that two years after treatment, 8% of patients who received HoLRP had required additional surgical treatment as compared to 12% of patients who had received TURP (not statistically significantly different).

- **One trial reported that some physiological measures are significantly better after HoLRP than after VLAP, but improvement in symptoms is similar. Catheterization times are shorter after HoLRP than after VLAP.**

Two trials compared HoLRP to VLAP.(86,120) Gilling et al. (1998)(120) (N = 22) found that some physiological measures were significantly better after HoLRP than after VLAP, but reported that symptoms and postvoid residual volumes were similar after these two treatments. The trial may not have been sufficiently powered to detect clinically meaningful differences. Both trials reported that catheterization times were significantly shorter after HoLRP than VLAP (1.4-1.9 days versus 9.0-11.9 days, respectively).(86,120)

Holmium Laser Enucleation of the Prostate (HoLEP)

Both trials of HoLEP used the VersaPulse holmium laser and VersaCut Morcellator (Lumenis, Santa Clara, CA, USA).

- **Two trials reported that after six months, HoLEP and open prostatectomy yield similar symptom improvement in patients with large prostates. Two trials reported that HoLEP required shorter hospital stays and one trial reported that HoLEP required shorter catheterization times.**

Trials of HoLEP enrolled only patients with large prostates (>100 grams), and therefore the control group surgical procedure was open prostatectomy. Two controlled trials (N = 140) reported on this comparison.(123,124) At six months, symptoms and physiological measures were similar after HoLEP and open prostatectomy.

Kuntz et al. (2002)(123) reported statistically significant longer operation times for HoLEP than for open prostatectomy (mean 136 minutes versus 91 minutes). Moody et al. (2001)(124) reported a difference in the same direction that was not statistically significant (HoLEP 197 minutes, open prostatectomy 173 minutes). Both trials reported that hospital stay was statistically significant shorter after HoLEP than after open prostatectomy (2.1-2.9 days vs. 6.1-10.5 days).(123,124) One trial reported that catheterization time was statistically significant shorter after HoLEP than after open prostatectomy (1.28 days vs. 8.1 days).(123,124) In addition, fewer HoLEP patients required blood transfusions (0% versus 13-30% for TURP).(123,124)

Both trials reported similar rates of adverse events for HoLEP and open prostatectomy, but few (usually <5) patients experienced any given event. Therefore, the frequencies of adverse events that were reported in these trials may not be reliable.

One trial reported that retreatment rates at six month followup were similar for HoLEP and prostatectomy,(123) but no data from controlled trials are currently available on long-term retreatment rates.

Interstitial laser coagulation

Technology Description and Clinical Issues

In interstitial laser coagulation (ILC), the physician inserts a fiberoptic laser probe through a cystoscope into the prostate at fixed points. Laser energy is applied for approximately three minutes to coagulate each area of obstructing prostate tissue, producing necrosis. In contrast to other laser procedures, where coagulation necrosis occurs at the urethral surface, in interstitial laser coagulation, delivery of laser energy directly into the tissues produces coagulation necrosis inside the adenoma. The postprocedural tissue sloughing that occurs following surface laser treatment does not occur with ILC,(125) which may reduce the risk of urinary tract infection.(126) The treated tissue then cavitates or is absorbed over a period of several weeks.

ILC can be performed in a physician's office or an outpatient surgery center using local anesthesia and intravenous sedation. The ILC procedure takes approximately 30 to 60 minutes, depending on the number of areas to be treated. Postprocedure catheterization is required for 7 to 21 days. The use of laser energy minimizes the risk of bleeding. However, like most other laser procedures, ILC destroys tissue, not reserving any for histological examination, and thus requires physicians to take pretreatment samples in patients at risk for prostate cancer.(127)

ILC was first developed using the Nd:YAG laser of 1,024 nm, but has since been modified for use with diode lasers of 805 to 980 nm.(126) Standard treatment protocol begins with the laser firing with 20 watts of energy, gradually decreased to about 7 watts. The applicator may allow laser energy to be emitted in all directions, or only circumferentially forward.(126) It is unclear from the small literature base whether these different technologies affect the efficacy of ILC; therefore, we discuss the reported efficacy of ILC as a group, which conforms to the way the procedure is categorized by clinicians in the literature. There are no published controlled trials comparing the efficacy

of individual ILC devices. The only application difference that we call out in our discussion is a single controlled trial of low-powered ILC, in which the initial wattage is lower than in the traditional protocol.(128) FDA cleared lasers used in ILC include the Ethicon Indigo 830e and Dornier's MediLas H. The use of these lasers is generally indicated for men over 50 years old with symptoms of BPH and prostatic lobes sizes of 28-85 cc.

Clinical Practice Guidelines

The Fifth ICBPH rated ILC an "acceptable" procedure for BPH.(19) The AUA considers ILC an "emerging therapy" and states that additional data are required before it can be recommended as a treatment option. However, they state that ILC may be offered to appropriate patients provided that the uncertainty of ILC outcomes relative to recommended treatments are discussed with the patient.(3)

Findings

Two of the five trials comparing ILC to TURP reported the device used: one trial used the Medilas 4199 Fibertom Nd:YAG laser (Dornier MedTech, Kennesaw, GA USA) at a wavelength of 1,064 nm. Wattage was varied from 20 W down to 7 W.(129) The second trial used the Dornier ITT thermotherapy fiber (Dornier MedTech), from 20W down to 7.5 watts.(127)

The other three studies did not specify what device was employed, but two of them reported starting the treatment at 20 watts.(43,126) Without further information or comparison among devices, we assume that this class of devices can be considered together.

- **ILC and TURP generally provide similar improvements in symptoms and quality of life. Results for physiological measures were mixed. Two trials reported higher retreatment rates after ILC. Unlike TURP, ILC may not require any hospitalization time, but this may be offset by a longer catheterization time.**

Two RCTs and three non-randomized controlled trials (N = 496) compared ILC to TURP.(43,126,127,129,130) In general these trials reported similar results for ILC and TURP in symptoms (IPSS) and quality of life; however, one study reported that DANPSS symptom and bother scores were higher (worse) after ILC than after TURP.(129) One trial asked patients about satisfaction with treatment: while 56% of TURP patients reported being "completely satisfied," only 24% of ILC patients reported the same.(129)

Results for physiological measures were mixed; two RCTs found that peak urinary flow (Qmax) was similar after ILC and TURP,(43,129) while two non randomized trials found Qmax to be better improved after TURP (statistical significance not reported).(126,127) One RCT and one non-randomized trial reported that post-void residual volume (PVR) was similar after both treatments,(43,127) while one RCT and one non-randomized trial found that PVR was higher after ILC (statistically significant in the RCT).(126,129)

The two trials that reported retreatment rates for ILC and TURP both found higher rates for ILC (7-16% ILC versus 0-3.5% TURP) (statistical significance not reported).(43,127) However, both studies had a small number of patients in the ILC group (N = 30 to 37), and the overall number of patients undergoing retreatment were very low (<4 per group). This low statistical power may result in unreliable event rate estimates.

Two RCTs reported that ILC had higher rates of urinary tract infections (UTI) (statistical significance not reported), (20-61% ILC versus 11-14% TURP)(43,129) while one non-randomized trial reported that ILC was associated with a lower rate of UTI (7% versus 13% for TURP).(127) Because these were not large trials, estimated event rates may not be reliable, especially for those events occurring with low frequency.

In the three studies reporting hospitalization time (two RCTs and one non-RCT), ILC had a shorter hospitalization time than TURP (and in the United States, may almost always be performed on an outpatient basis(131)),(43,127,129) but one non-randomized trial reported that ILC requires several days of catheterization instead (mean: 14 days versus 3.5 days).(127)

- **Two trials reported that ILC and transurethral microwave therapy (TUMT) yield similar symptom improvements, but that ILC provided higher peak urinary flow rates. One RCT also reported that ILC was associated with a higher rate of adverse events than TUMT.**

Two trials, Norby et al. (2002) and Arai et al. (2000) (N = 182) compared ILC to TUMT.(129,130) Norby's randomized trial reported similar symptom improvements for ILC and TUMT at 6 months and slightly more improvement in peak urinary flow rate (Qmax) with ILC (statistical significance not reported).(129) The Arai trial, which was not randomized, reported significantly greater improvements with ILC for symptoms, Qmax and QoL; however, the study was not randomized and had only 3 months' followup.(130)

Norby reported in general that there were more adverse events after ILC than after TUMT, including UTI (61% versus 30%), re-retention (9% versus 2%), retrograde ejaculation (35% versus 22%), and decreased erectile capacity (29% versus 9%) (statistical significance not reported). In one trial, ILC required a mean of 3 days of hospitalization, versus no hospitalization for TUMT.(129)

- **One non-randomized controlled trial reported that ILC resulted in better symptomatic, quality of life, and physiological improvements than radio frequency needle ablation (RFNA).**

Arai et al. (2000),(130) (N = 88), was the only trial to compare ILC to RFNA (also known as TUNA®), in a non-randomized prospective trial. After three months, ILC was found to be significantly superior to RFNA in terms of IPSS scores, quality of life, and post-void residual volume. Similar improvements were noted for the two groups in terms of BPH Impact Index and maximum urinary flow. Retreatment rates were not reported.

- **One non-randomized controlled trial reported that ILC resulted in similar symptomatic improvements to hybrid laser, and a lower retreatment rate.**

Pypno et al. (2000) (N = 142), compared ILC to both hybrid laser (VLAP) and TURP. Only 30 patients were included in the ILC treatment group, which limits the statistical power of this comparison. In looking only at results up to six months when most patients were still enrolled, symptom scores, Qmax, and post-void residual volume were all similarly improved in both groups. After a mean 23 months of followup, more hybrid laser patients required retreatment than did patients receiving ILC (15% versus 7%).(127) No statistical analyses were provided to validate any of the patterns observed.

- **One RCT reported that low-energy ILC is not as effective as TURP in terms of symptoms, quality of life, or physiological measures. This one trial also reported that while low-energy ILC has a lower rate of retrograde ejaculation than TURP, UTI rates were similar for the two treatments. One trial reported that catheterization time was longer after ILC.**

Martenson et al. (1999)(128) (N = 44) compared ILC using a diode laser to apply low energy (10 watts maximum, device not described) to TURP. Results suggested that low-energy ILC was not as efficacious as TURP in terms of most quality of life, symptoms, and physiological measures. It was associated with a lower rate of retrograde ejaculation (42% versus 75%). Catheterization time was 27 days for ILC versus 3 days for TURP, not offset by the reported hospitalization times (2.3 versus 3.8 days). (However, ILC is almost always performed on an outpatient basis in the United States,(131) therefore these statistics may not be representative of general practice.) Twenty percent of patients (6 patients) were retreated in the low-ILC group, versus 7% (one patient) in the TURP group (not a statistically significant difference in this low-powered trial).

Hybrid laser techniques

Technology Description and Clinical Issues

Hybrid laser procedures involve the use of one or more laser techniques, types, and power settings to treat BPH. For example, one hybrid technique uses non-contact VLAP with an Nd:YAG laser and sidefiring fiber to coagulate prostate tissue followed by CLAP using a contact laser probe to vaporize the tissue. Another hybrid technique uses a KTP laser at 34 W for bladder neck incision followed by Nd:YAG coagulation at 60 W.

Hybrid laser techniques were developed to reduce side effects associated with certain laser wavelengths. Using a KTP/Nd:YAG hybrid technique, for example, allows the surgeon to vaporize sections of Nd:YAG coagulated tissue with the KTP laser to reduce the likelihood of prolonged postoperative urinary retention and catheterization.

These techniques employ the same devices as other laser techniques, thus the same FDA 510(k) clearances for marketing apply.

Clinical Practice Guidelines

No current clinical practice guidelines discuss hybrid laser techniques.

Findings

Seven controlled trials (N = 961; published in 11 reports) have investigated hybrid laser techniques.(109,112,127,132-139) Four trials compared a hybrid laser technique to TURP, and three trials compared a hybrid laser technique to other surgical procedures.

Three studies(91,109,135) used the ADDstat fiber (Laserscope, San Jose, CA, USA), one(112) used the Urolase fiber (Bard, Covington, GA, USA), one(139) used three different fibers (SideFire, Slimline, and DuoTome SideLite, all manufactured by Lumenis, Santa Clara, CA, USA), and two(127,133) did not report the specific type(s) of laser fibers. Also, the seven controlled trials used six different laser generators; these included the VersaPulse Select laser (Lumenis, Santa Clara, CA, USA),(139) the Nd:YAG/KTP laser (Laserscope, San Jose, CA, USA),(109,135) the KTP/YAG XP laser (Laserscope, San Jose, CA, USA),(137) the Nd:YAG Medilas 4060 Fibertom laser (Dornier, Munich, Germany),(127) the SLT Nd:YAG laser (Surgical Laser Technologies, Oaks, PA, USA),(133) and an Nd:YAG laser from an unspecified manufacturer.(112)

- **Hybrid laser techniques are too varied to permit general conclusions about this category of treatment for BPH.**

Comparisons between hybrid laser techniques and TURP

In one trial (N = 100), surgeons first vaporized the prostatic fossa using a KTP laser, and then performed VLAP using an Nd:YAG laser to create craters in the lateral lobes.(109,132,137,138) The authors reported that symptoms, physiological measures, and retreatment rates were similar for the hybrid laser technique and TURP at three to six years' followup. Two other trials, one randomized and one not, (N = 275) compared outcomes of patients who received TURP to those who received a hybrid technique consisting of VLAP followed by CLAP.(127,133,134) The authors of both trials reported that patients fared better after TURP.

A fourth trial (N = 204) used a hybrid technique with the KTP laser for vaporization and then the VLAP-free paint technique for coagulation, compared to TURP.(112,120) At one year after treatment, authors reported no differences between patients who had this hybrid technique and the patients who had received TURP.

These four trials suggest that the techniques and results for comparison of hybrid laser to TURP have varied too widely to consider the studies as a group to reach conclusions about one "hybrid" technique.

Comparisons between hybrid laser techniques and other surgical procedures

One trial (N = 31) compared outcomes after TUEVP to those after the KTP/VLAP technique described above, (137,138) and reported similar outcomes at six months with respect to symptoms, physiological measures, and adverse events. However, the authors did report that operation time was shorter for the hybrid laser technique than for TUEVP.

A non-randomized trial (N = 142) compared the perioperative outcomes of a combined technique of HoLAP and VLAP with those of HoLAP alone, and reported shorter

catheterization times and lower recatheterization rates for patients receiving HoLAP alone.(136)

One RCT compared VLAP with the Urolase fiber to those after CLAP/VLAP with the Ultraline fiber.(135) Authors reported no significant differences between the two laser techniques at three years after treatment.

As with the comparison to TURP, again this literature demonstrates a wide variety of hybrid techniques that preclude coming to conclusions about hybrid laser treatment as a single group.

Photoselective vaporization of the prostate (PVP)

Technology Description and Clinical Issues

PVP uses a potassium-titanyl-phosphate (KTP) laser at 80 watts to vaporize prostate tissue. PVP has been under investigation for about five years, and the first commercially available PVP laser system for BPH treatment was introduced in early 2002.(140) PVP was developed in response to the side effects associated with the deep tissue coagulation produced by Nd:YAG lasers. KTP laser wavelengths penetrate only 1 to 2 mm, and the vaporization process may help avoid the perioperative side effects (such as tissue sloughing) of other laser surgical procedures. Another potential advantage of PVP is low blood loss, which can be a problem with TURP.

The PVP procedure lasts from 20 to 50 minutes, depending on prostate size, and is performed using local anesthesia, intravenous sedation, or general anesthesia on an outpatient basis or with an overnight stay.(140) PVP has been used to treat prostates up to 120 grams in size.

PVP using the Lyra G Series Surgical Laser System (Laserscope, San Jose, CA) has received FDA 510(k) clearance to be marketed for the treatment of BPH. The approval documentation did not mention specific indications for prostate size.

Clinical Practice Guidelines

Since it has only recently been introduced, PVP was not addressed in the Fifth ICBPH, EAU, and AUA guidelines. We identified no other guidelines addressing this technology.

Findings

Our searches identified no controlled comparisons of PVP to sham or to other treatments.

Minimally Invasive Treatments

Transurethral radiofrequency needle ablation (RFNA or TUNA®)

Technology Description and Clinical Issues

RFNA (marketed in the United States under the trade name, TUNA®) is a minimally invasive technique that uses low-level radiofrequency (RF) energy to ablate selected areas of prostate tissue. An RFNA system consists of a computerized RF generator and a urethral catheter with two needles at the tip. The needles can be deployed in the urethra independently, and can be positioned at either lateral lobe of the prostate. The RF generator produces a dual 465 kilohertz RF signal that is transmitted through the catheter to each of the needles to deliver energy at a power between 2 W and 15 W, thereby heating the defined tissue area to produce coagulative necrosis. Thermosensors located in the protective nylon shields of the needles and in the side of the catheter tip monitor temperatures at the periphery of the treated area and in the urethra. The TUNA® system has a safety feature that will automatically shut off the RF signal when the tissue impedance exceeds 400 ohms or the urethral temperature exceeds 46 degrees Celsius.(141,142) The amount of tissue ablation is determined by the length of the needles (tissue contact), power delivery, and treatment duration.(143)

RFNA has been used for prostates ranging in weight from 15 to 100 grams.(144) The procedure takes approximately 45 minutes and can be usually performed in a physician's office or as an outpatient procedure with topical or local anesthesia, although some patients may require additional sedation.(145) Patients are able to return to most normal activities within 24 hours.(146)

Medtronic Corporation manufactures the TUNA® system and is the only company with FDA clearance to market such a system in the United States. It is cleared for use in men over the age of 50 years with prostate volume of 20-50 cc, who are experiencing symptoms due to urinary flow obstruction secondary to BPH.

Clinical Practice Guidelines

The Fifth ICBPH has noted that RFNA could become a "treatment of choice" for relieving BPH symptoms in elderly patients at high surgical risk. However, they emphasized that patient selection and degree of obstruction are critical factors, since RFNA appears to be effective for patients with mild to moderate obstruction, but results have been less than satisfactory for patients with more severe obstruction.(19)

In 2001, the EAU concluded that RFNA is a "simple and safe technique," but does not recommend it as a first-line treatment for patients with BPH due to treatment failure rates.(49) In 2003, the AUA concluded that RFNA is an effective treatment for partially relieving BPH symptoms (though not as effective as TURP), and that the ideal patient has obstructive BPH, predominantly lateral lobe enlargement, and a prostate size of 60 grams or less.(3)

Findings

Few details are provided by the available articles on the devices and techniques used to perform RFNA. None of the published trials appeared to use the FDA cleared TUNA® system, and it is not clear whether there are clinically meaningful differences among techniques. Without any direct comparison of techniques, we assume they are similar and discuss all four studies as a group.

Two randomized controlled trials (Bruskewitz et al. 1998; Mostafid et al., 1997) and two non-randomized comparative studies (Arai et al., 2000; Schatzl et al. 2000), (N = 330) compared RFNA (using the TUNA system) to TURP.(63,64,130,147-149)[4]

Schatzl also compared RFNA to TUEVP, HIFU, and VLAP, while Arai also compared it to ILC and TUMT. However, in both these latter studies, patients were often assigned to a treatment out of personal preference or based on physiological variables; thus, treatment groups may not be comparable. The Schatzl study also has limited statistical power (approximately 15 patients per treatment group), and may not be able to identify clinically significant differences between the groups.

- **RFNA results in less symptom and physiological improvement than TURP up to 24 months after treatment, and two trials reported that the two treatments have similar effects on quality of life. One trial reported that decreased ejaculate and retrograde ejaculation occur less often after RFNA than after TURP.**

Bruskewitz et al (1998)(147,148) (N = 121) and Mostafid et al. (1997)(149) (N = 50), both randomized controlled trials, found that IPSS scores and Qmax improved significantly more after TURP than after RFNA. In the Bruskewitz trial (1998)(147,148) these differences did not become apparent until 12 months after treatment. One trial reported that quality of life scores were similar; 50% or better improvement in the AUA bother score occurred in 65% (38/59) of RFNA patients and 75% (35/47) of TURP patients (not statistically significant).(147)

The results from the study of Arai et al. (2000),(130) a non-randomized prospective trial (N = 116), generally agree with the findings of the above two RCTs.

All four trials reported some adverse events. In the largest RCT (N = 121), Bruskewitz reported that all adverse events occurred less often after RFNA than after TURP (statistical significance not reported): decreased ejaculate occurred in 13% of RFNA patients and 54% of TURP patients; bleeding occurred in 32% and 100%, respectively; erectile dysfunction in 0% and 13%; and retrograde ejaculation in 0% and 38%.(147,148)

The Mostafid and Schatzl trials enrolled too few patients to provide reliable adverse event rates. They report the occurrence of UTI, dysuria, and urinary retention in the RFNA group, and blood transfusion, UTI, and urinary retention in the TURP group.(64,149) Arai et al. (2000) reported only sexual complications; the authors asked

[4] Bruskewitz and colleagues have recently published follow-up data to their 1998 study following patients to five years (Hill et al., 2004), but results beyond two years had a high attrition rate (>30%) and cannot be considered reliable.(150)

patients about ejaculation after treatment; significantly more patients undergoing TURP had had no ejaculate or severely or moderately decreased ejaculate after treatment (69% vs 46%, statistically significant).(130)

Bruskewitz (1998) reported that operation time was similar for RFNA and TURP (mean 42 and 53 minutes, respectively). All 56 TURP patients required catheterization while only 40% (26/65) of RFNA patients did (statistical significance not reported).(147,148) Hospitalization was slightly shorter for the RFNA group according to Bruskewitz and Schatzl (1-1.5 days for RFNA and 2.1-4.3 days for TURP).(63,64,147,148) More patients in the TURP group required blood transfusions (14%, or 3/22 versus 0%, or 0/20) in the Mostafid trial (statistical significance not reported).(149)

There are not enough data from controlled trials to determine rates of retreatment.

- **One non-randomized trial reported that RFNA and TUMT provide similar results, although patients may be more satisfied with RFNA. One trial reports that RFNA is not as effective as ILC.**

Two studies (N = 185) compared RFNA to a variety of competing minimally invasive surgeries.(63,64,130) One study by Schatzl (2000)(63,64) (N = 46) compared RFNA to TURP, TUVP, HIFU, and VLAP. However, sample sizes for each treatment group were small ($n \leq 15$), so this study may not have had the power to detect statistically significant differences. Patients were also not randomized to treatment, which may have resulted in non-comparable groups.

In another non-randomized trial, Arai et al. (2000)(130) (N = 139) compared RNFA to both ILC and TUMT. Subjective measures improved after both RFNA and TUMT, although physiologic measurements showed no significant change. When asked about satisfaction with treatment, 23 out of 42 (55%) RFNA patients and 8 out of 40 (20%) TUMT patients were “delighted” or “pleased” (statistical significance not reported).

High-intensity focused ultrasound (HIFU)

Technology Description and Clinical Issues

HIFU is a minimally invasive procedure that uses a transrectal ultrasound probe to image the prostate and then heat tissue to 70 degrees to 90 degrees Celsius without harming adjacent healthy tissue. The physician uses ultrasound guidance to position the HIFU transducer and ensure that the prostatic urethra and bladder neck are in the treatment zone. The transducer is designed to rotate laterally to treat seven to nine areas of the prostate. HIFU treatment causes coagulative necrosis of the prostate tissue. In contrast to other treatments, the HIFU device is inserted rectally and so does not contact the prostate or urethra. This eliminates risks associated with device-related urethral and intraprostatic manipulation.

The outpatient HIFU procedure usually takes less than three hours, and is performed under general or spinal anesthesia, or intravenous sedation, depending on the patient. Postprocedure catheterization time ranges from a few days to over a week.

The ultrasound device (Focus Surgery Sonoblate 500) used for HIFU treatment of the prostate is currently under investigation in the United States, and is not approved or cleared by the FDA for marketing.(151)

Clinical Practice Guidelines

The EAU does not recommend HIFU for elderly patients.(49) Information about HIFU was not included in the 2000-2001 Fifth ICBPH proceedings. The AUA considers HIFU an "investigational therapy" that should only be offered in the context of a clinical trial.(3)

Findings

- **Only one study examined HIFU, but it was not randomized, and patients in its groups were not comparable.**

A trial by Schatzl et al (2000)(63,64) was the only comparative study of HIFU. It compared HIFU to TURP, TUEVP, VLAP and RNFA. Randomization was attempted, but could not be carried out, because patient characteristics such as prostate size, prostatic calcifications and middle lobes limited the types of patients who could receive the different treatments. The patients who received HIFU tended to have smaller prostates and less severe symptoms than those who received TURP. Results may be influenced by these differences in patients, and are not considered further.

Transurethral microwave thermotherapy (TUMT)

Technology Description and Clinical Issues

TUMT is a nonsurgical, catheter-based treatment that uses radiant microwave heating to ablate prostate tissue. The microwave generator delivers energy through a urethral catheter to heat the prostate tissue to between 45 degrees and 55 degrees Celsius, and the heating process causes necrosis (localized tissue death) of the prostate tissue that is obstructing the urethra. It is performed on an outpatient basis and usually takes about an hour. Postoperative catheterization times can range from a few days to several weeks, depending on the degree of prostatic edema.(6) Because it does not cut out tissue, there is no reserved tissue for histological examination for prostate cancer.

Although all TUMT devices are designed to deliver microwave energy to the prostate via a urethral catheter, currently manufactured devices differ on a variety of technical details. For example, the standard TUMT method, no matter which device is used, generally takes about one hour to perform. However, two devices have been introduced or modified recently to perform the procedure in about 30 minutes.(152,153) There are currently no published controlled trials about the efficacy of these 30 minute protocols. Although it is possible that individual devices and protocols may differ in level of efficacy, there is no published evidence from controlled trials comparing different TUMT devices in terms of patient outcomes.

Another difference among some TUMT devices is their intended patient population. Some manufacturers state that their devices are for patients with "symptomatic" BPH, and work by heating and destroying prostate tissues (e.g., Prostatron 2.0). Other

manufacturers state that their devices are for patients with "obstructive" BPH and focus the thermotherapy on the bladder neck where the obstruction occurs (e.g., Prostatron 2.5).(154)

One major delineation between different TUMT devices is the presence or absence of a cooling mechanism. There are four TUMT devices market approved by FDA that incorporate a urethral cooling device that protects the urethra from the extreme temperatures used to destroy prostatic tissue, and are intended to provide a more tolerable level of pain to the patient.(155) These are the Targis® and Prostatron® (2.0 and 2.5), both manufactured by Urologix, Inc., the Prolieve™ manufactured by Celsion Corporation (on which no published data are yet available), and the Urowave® manufactured by Dornier, Inc. (The Urowave is not currently marketed within the United States.) Two other devices marketed within the U.S. (TherMatrx TRX-2000; Prostalund CoreTherm™) do not incorporate a cooling mechanism, under the supposition by the manufacturers that such a mechanism did not achieve its goal of patient tolerance, and as a result requires heavy patient sedation, which has potential side effects. The non-cooling devices are reported to require only light patient sedation.(155)

Grouping TUMT devices based on the presence or absence of a cooling mechanism is a widely accepted classification in the industry. Given the technical differences between cooling and non-cooling devices, we consider the results from trials on these two classes of TUMT device separately.

We discuss the reported efficacy of all cooling devices as a single group, and there is no published evidence from controlled trials that the individual devices differ in any clinically significant way. The same holds true for the non-cooling devices, although less evidence is available on this newer technological approach.

Treatment efficacy may also be affected by the intraprostatic temperature achieved during treatment.(156) The target temperature of the prostate during TUMT has been reported in clinical trials to range from 45 to 55° C. However, details on target or maximum allowed temperature were scarce in the literature, thus precluding us from analyzing results based on this treatment characteristic. There appear to be no trials that have analyzed the target temperature and its effect on clinical outcomes after TUMT.

The wattage used to attain therapeutic prostatic temperatures may also affect the performance of the device, as different devices are designed to use different power levels. For example, while the Prostatron 2.5 can deliver up to 70 watts of energy, the Thermatrx 2000 delivers only 7 watts. The lack of a cooling mechanism in the Thermatrx device may allow it to heat the tissue as quickly to high temperatures as do cooling devices, even though the actual amount of power used is much lower. We were able to locate only a single, non-randomized controlled trial in the published literature (Rivas et al., 2000) that compared higher and lower-wattage devices in terms of clinical outcomes; however, in this study, patients with smaller prostates were more likely to be assigned to the low-power group, and those with large prostates to the high-power group.(157) Thus, these results may be unreliable. Hence, we have no information on how the wattage of the

device may affect the outcomes of treatment, and do not analyze results based on energy level.

The specific design and performance characteristics of the antenna used to deliver the microwave energy to the prostate may also play a critical role in achieving therapeutic intraprostatic temperatures during TUMT, and one laboratory study has shown that different device antennas do provide different patterns of energy to the targeted tissue.(156) However, such findings have not been directly linked to clinical outcomes, and therefore such device specifications are not addressed further in our consideration of the evidence on TUMT.

In October 2000, the U.S. Food and Drug Administration issued a hazard warning for TUMT based on reports of thermal injuries that required subsequent colostomies, partial amputation of the penis, or other interventions. According to FDA,(158) these injuries may take hours or days to become apparent, and are a result of incorrect device placement or migration, balloon leakage, failure to pause treatment when the patient signals pain, oversedation of the patient, treatment of prostates larger than those specified in product labeling, and treatment of patients who have undergone pelvic radiation therapy. This warning appears to apply to cooling TUMT devices, which were the most common TUMT devices on the market at the time of the hazard warning. No such adverse events were reported in the clinical trials considered in this report below; however, clinical trials may provide more rigorously controlled treatment methods than are performed in general practice.

Clinical Practice Guidelines

In 2001, the World Health Organization Committee on Interventional Therapies recommended the use of TUMT as a minimally invasive treatment alternative for BPH.(38,48) The EAU guidelines recommend TUMT for patients with larger prostates and higher grades of bladder outlet obstruction, and for patients who wish to avoid surgery or who no longer respond favorably to medical management.(49)

The Fifth ICBPH stated that TUMT is a viable BPH treatment that has "gained a firm place in the urologist's armamentarium."(19) In addition, the ICBPH highlighted the importance of mapping intraprostatic temperature during TUMT to avoid thermal injury, and that TUMT systems should have some method of assessing temperature during treatment.(19) All FDA-cleared devices considered in the present report have built-in temperature monitors and safety shut-off mechanisms intended to prevent unnecessary thermal damage.

The AUA concluded that TUMT is effective in partially relieving BPH symptoms, and that no commercial device is superior to another, because their literature searches found no direct comparator trials of commercial devices.(3) ECRI concurs that no such comparison trials are available currently in the published literature, up to May 2003.

Findings

Here, we present results from trials of cooling and non-cooling devices separately, as this is an accepted delineation in the industry, and because no other clinical data exist that would support an alternative approach for examining differential efficacy of the devices. We focused on trials that provided technical information about the devices they used, or used a device approved for marketing by FDA. We do not discuss studies that did not identify the type of device used.(159-167)

Thirteen of the 15 relevant controlled trials we identified randomized patients to treatment groups (RCTs),(129,159,168-179) and two were non-randomized controlled trials.(130,157)

Cooling TUMT

- **Cooling TUMT leads to improved symptoms and physiological measures up to 12 months after treatment.**

Five sham-controlled trials (N = 674), all of which blinded patients to treatment, evaluated TUMT devices that employed a urethral cooling mechanism (Targis; Prostatron; Urowave).(159,168-172) All trials were randomized. Four (N = 554) found cooling TUMT to be significantly more effective than a sham treatment in terms of symptoms and physiological measures.(159,168-171) Results on TUMT's effects on quality of life were mixed. A fifth trial (Nawrocki et al., 1997, N = 120) found similar results on all outcome measures for the sham and TUMT groups. Through an analysis with an additional no-treatment group, the authors attributed many improvements exhibited by both the TUMT and the sham groups to a placebo effect.(172) Improvements may also have been due to the placement of the catheter by itself.

Although individual devices may differ in technical specifications, it appears from the above trials that cooling TUMT devices show the same general trend of results.

Given that cooling TUMT has been found to be generally more effective than a sham treatment (although the precise reason for its efficacy is unclear), it is important to determine whether it offers any advantages over TURP, the current standard of care. The most obvious advantage of TUMT is that it is performed on an outpatient basis under mild sedation. Thus, TUMT is initially less invasive than TURP in the patient's daily life.

- **Most trials report that cooling TUMT provides less symptom relief and less improvement in physiological measures than does TURP. One trial reported that retrograde ejaculation was less common after TUMT than after TURP. Retreatment rates may be higher after cooling TUMT than after TURP.**

Five RCTs and one non-randomized controlled trial (N = 514) compared cooling TUMT to TURP.(129,130,173-176,180-182) Three trials on recent models of the Prostatron(129,173,174,180-182) (N = 267) reported that symptoms improved significantly less after TUMT than after TURP. In one trial, more TURP patients expressed satisfaction with treatment after six months (54% vs 16% for TUMT).(129)

However, two older trials (N = 132) using earlier versions of Prostatron(175,176) found TURP to be more effective than TUMT on physiological outcome measures such as Qmax, but reported that the two technologies resulted in similar scores most symptom scales, such as IPSS and Madsen-Iverson.

Adverse events may be more severe after TURP than after cooling TUMT; however, the only device for which adverse event data are available is the Prostatron. Ahmed et al. (1997) reported that more TURP patients experienced retrograde ejaculation after treatment than did TUMT patients (63% versus 22%).(175) Dahlstrand et al. (1995) reported more "late complications" after TURP than after TUMT (13% versus 0%).(176) Norby et al. (2002)(129) reported that the most common adverse event for TURP or TUIP was retrograde ejaculation (50% of patients questioned) and for TUMT, UTI (30% of patients evaluated).

Three trials evaluating Prostatron 2.0 (60W) or 2.5 (70W) reported that retreatment rates may be higher after cooling TUMT than after TURP.(174,176,180) At 36 months, Floratos et al. (2001) employed Kaplan-Meier statistics to estimate the retreatment rate to be 20% for the TUMT group and 13% for the TURP group (not statistically significant).(180) At 30 months, D'Ancona et al. (1998) reported a similar pattern, with retreatment rates of 26% (8/31) for the TUMT group and 10% (2/21) for the TURP group (statistical significance not reported).(174) At 24 months, Dahlstrand also reported that retreatment rates tended to be higher after cooling TUMT (11%, 4/37 patients) than after TURP (0/32 patients) (statistical significance not reported).

- **One trial reported that cooling TUMT yielded more improvements in symptoms, quality of life, and peak urinary flow rate than alpha-blockade medication.**

In a single randomized controlled trial (N = 103), Djavan et al. (2000)(179) compared cooling TUMT using the Targis device to the alpha-blockade drug, Terazosin, given in increasing doses (from 1 to 5 mg) for 24 days. Patients in this trial had moderate to severe LUTS. The authors postulated that TUMT might provide a viable treatment to delay symptom onset compared to alpha blockades, which have side effects. Over six month followup, patients showed greater improvements in the TUMT group as measured by symptom scales (IPSS), quality of life, and peak urinary flow rate. The actuarial failure rate was significantly lower in the TUMT group (6% versus 41%). Adverse events experienced by patients undergoing TUMT included UTI and loss of ejaculate (exact rates not reported). The Terazosin patients experienced dizziness, asthenia, and headaches (exact rates not reported).

- **Two trials provided mixed results as to the relative efficacy of cooling TUMT compared to ILC, suggesting that TUMT is either equally effective or less effective than ILC. One trial reported that fewer patients were satisfied with cooling TUMT treatment than with ILC or RFNA.**

One RCT (Norby et al. 2002) (N = 94) compared cooling TUMT using the Prostatron 2.0 device to ILC, and reported similar improvements in symptoms, quality of life, and physiological measures.(129) In a non-randomized trial, Arai et al. (2000) (N = 88) compared cooling TUMT (using the Dornier Urowave) to interstitial laser coagulation

(ILC) and radiofrequency needle ablation (RFNA, or TUNA®); ILC appeared to provide more favorable results than TUMT on all reported outcome measures. Results were similar for RFNA and TUMT, although more RFNA patients were satisfied with treatment (55% versus 24%).(130) Significantly more ILC patients than TUMT patients reported being "delighted" or "pleased" (74% versus 24%).(130)

Non-Cooling TUMT

- **One RCT reported that non-cooling TUMT may improve symptoms but has associated adverse events.**

One published blinded, multicenter RCT (Albala et al., 2000) (N = 190) compared a non-cooling TUMT device (TherMatrx 2000) to a sham treatment.(177) Non-cooling TUMT improved symptoms more than did sham treatment, but was also accompanied by certain adverse events, including bladder spasm (4.1%), gross hematuria (9.1%), and a need for recatheterization (16.8%patients).(177)

- **One RCT reported that non-cooling TUMT and TURP yield similar improvements in symptoms and physiological measures, and each has different adverse events.**

Wagrell et al. (2002)(178) compared non-cooling TUMT to TURP (N = 146). They found that TUMT and TURP provided similar results in all symptom and physiological measures after 12 months. TUMT patients experienced less hematuria (13% versus 39% of patients) and transient incontinence (3% versus 13%) than TURP patients, but more micturition urgency (37% versus 13%) that continued up to 12 months. Catheterization time was longer for TUMT than for TURP (14 versus 3 days), but this is offset by the lack of hospitalization time with TUMT (0 versus 5 days).

Transurethral thermotherapy (TUT)

Technology Description and Clinical Issues

Thermotherapy is distinguished from hyperthermia by the maximum temperature achieved.(3,183) In thermotherapy treatments, prostate temperatures range from 45 degrees to 60 degrees Celsius; in thermotherapy treatments, temperatures range from 41 degrees to 44 degrees Celsius. Tissue coagulation is known to occur at temperatures greater than 45 degrees to 50 degrees Celsius, but no clear prostate tissue effects have been demonstrated for temperatures below 45 degrees Celsius.(3)

Transurethral thermotherapy appears to be a precursor to the development of transurethral microwave thermotherapy, and was reported on in two controlled trials in 1991.(184,185) No technical details were provided in either trial, and the term "transuretheral thermotherapy" has not been used in the published literature since.

Clinical Practice Guidelines

The term "transurethral thermotherapy" is not mentioned in any current clinical practice guideline. The current technology used is transurethral microwave thermotherapy (TUMT), which is covered in a separate section of this report.

Findings

Because this treatment is outdated, we do not further consider the results of controlled trials on it.

Transrectal hyperthermia (TRH)

Technology Description and Clinical Issues

Hyperthermia is distinguished from thermotherapy by the maximum temperature achieved.(3,183) In hyperthermia treatments, prostate temperatures range from 41 degrees to 44 degrees Celsius; in thermotherapy treatments, temperatures range from 45 degrees to 60 degrees Celsius. Tissue coagulation is known to occur at temperatures greater than 45 degrees to 50 degrees Celsius, but no clear prostate tissue effects have been demonstrated for temperatures below 45 degrees Celsius.(3)

Transrectal microwave hyperthermia (TRH), also called localized deep microwave hyperthermia, uses a rectal applicator to heat prostate tissue to 42 to 44 degrees Celsius. The applicator is connected to a microwave generator (915 MHz, 20-60 W). A cooling system is used to control rectal wall temperature, and a computer system is used for data collection and analysis. Urethral temperature is monitored using a thermosensor contained in a specially designed urethral catheter, and rectal temperature is monitored using a thermosensor in the microwave applicator. During treatment, the maximum prostate temperature is continuously monitored using the rectal and urethral measurements.

Transrectal hyperthermia is performed on an outpatient basis and does not require sedation or anesthesia. Treatment lasts approximately 60 minutes and requires multiple sessions, usually once or twice weekly for several weeks. Transrectal hyperthermia is typically delivered in 6 to 10 sessions. However, clinical studies have reported delivery ranging from 3 to 18 treatment sessions.(186-188)

Transrectal hyperthermia was under investigation for BPH treatment up to the early to mid 1990s for patients who refused surgery or were at risk for surgical complications. Two controlled trials compared TRH to transurethral thermotherapy,(184,185) while one of these trials also compared it to a prostatic wall stent and prostatic spiral stent.(185) However, no controlled trials were ever published evaluating TRH relative to TURP or any other established treatment method. Although it has applications in treating cancer, transrectal hyperthermia is considered an outdated treatment for BPH.(183)

Clinical Practice Guidelines

Transrectal hyperthermia is not included in any current BPH clinical guidelines. It is therefore not considered further in this evidence report.

Findings

Because this treatment is outdated, we do not further consider the results of controlled trials on it.

Balloon dilation

Technology Description and Clinical Issues

Balloon dilation for BPH is similar to balloon angioplasty for coronary artery disease. A balloon is inserted into the prostatic channel, guided by a scope or the surgeon's finger, and then inflated. The inflation results in the tearing of prostate gland tissue, which allows passage of urine. Balloon dilation had been considered an alternative to open prostatectomy for the past several years, but has been abandoned because patients often have symptom recurrence and require retreatment within two years. In addition, the procedure is not effective for patients with larger prostate glands.(189)

Clinical Practice Guidelines

In a 1997 guideline, the World Health Organization classified balloon dilation as an unacceptable treatment for BPH.(190) The ICBPH has rated balloon dilation as an unacceptable treatment since 1995.(19) The AUA states that balloon dilation is "not recommended" for treatment of BPH.(3)

Findings

Because this treatment is outdated, we do not further consider the results of controlled trials on it.

Water-induced thermotherapy (WIT)

Technology Description and Clinical Issues

In WIT, also called balloon thermoablation or liquid ablation, heated water is circulated through a balloon that spans the prostatic urethra. There is a console heating system that heats and maintains water temperature at a chosen temperature between 60 or 70 degrees Celsius, and a peristaltic pump that continuously circulates the water. Usually, WIT protocols use water heated to 60 or 62 degrees Celsius. The circulating water inflates the balloon and conductively heats the prostate tissue, thereby causing coagulation necrosis. During WIT, urethral and rectal temperatures are monitored using temperature sensors. Because the treatment balloon length and catheter length are available in nine lengths, WIT can be used to treat prostates of varying sizes.(191)

WIT can be performed on an outpatient basis with local analgesia (lidocaine gel). The procedure takes approximately 45 minutes. In clinical studies, long catheterization times (weeks) or placement of temporary urethral stents were necessary. WIT is not considered an alternative to TURP in patients who can undergo TURP.(191) Rather, it is an option for patients at high risk for surgical complications, such as cardiopulmonary problems, or for patients who may require a less invasive treatment.

Although the device (Aquatherm, ACMI; previously Thermoflex, ArgoMed) is FDA-cleared for marketing, WIT is still being researched, since few clinical studies have been published and the protocol (treatment time and temperature) have not been supported by adequate pathologic studies.(192)

Clinical Practice Guidelines

In 2000, WIT was added to the list of interventional therapies evaluated by the ICBPH. The Fifth ICBPH noted that preliminary results of WIT are encouraging, but that further research is needed before clinical acceptance.(19) The AUA considers WIT an "emerging therapy" and states that additional data are required before WIT can be recommended as a treatment option. WIT can be offered to appropriate patients, provided outcomes relative to recommended treatments are discussed with the patient.(3)

Findings

Our searches identified no controlled comparisons of water induced thermotherapy (WIT) to controls or to other treatments.

Transurethral ethanol ablation

Technology Description and Clinical Issues

Transurethral ethanol ablation, also called absolute ethanol injection, transurethral injection therapy, or chemoablation, involves the injection of absolute alcohol into the prostate lobes. A physician inserts an endoscopic injection device into the urethra via a cystoscope. The needle tip is pushed through the urethral wall into the prostate tissue and alcohol is injected at two to five points, depending on the size of the prostate. The injection induces sclerosis and necrosis of the obstructing prostate tissue.

Transurethral ethanol ablation is an outpatient procedure usually performed in about 30 minutes with local anesthesia and/or intravenous sedation. Postprocedural catheterization for one to two days is required. Minor side effects include dysuria and hematuria.

In 1998 and 2000, endoscopic injection devices received FDA clearance for the injection of biomaterials into the urethra and lower urinary tract. However, the use of absolute alcohol for BPH has not received specific approval and is currently in clinical trials.(193) The AUA considers ethanol treatment an "investigational therapy" and states that it should not be offered outside the context of a clinical trial.(3)

Findings

Our searches identified no controlled comparisons of ethanol ablation to controls or to other treatments.

Prostatic stents

Technology Description and Clinical Issues

Prostatic stents are spring- or coil-shaped wire devices placed in the prostate channel to keep it open. The stent's insertion into the prostatic urethra pushes away obstructive tissue. Stents do not normally compete with surgical procedures and all of the less invasive devices, rather stents are typically used for patients who are not candidates for the other procedures and devices. Stent insertion takes approximately 30 minutes under local anesthesia. Thus, stents have been used in patients who cannot tolerate a surgical

procedure with general or regional anesthesia due to another medical condition. Stents are most commonly inserted in frail, elderly patients.(194) Problems associated with the use of these stents include irritation and debris accumulation around the stent, stent migration, and increased incidence of urinary tract infections.

As of July 2003, one prostatic stent (Urolome™) was FDA approved for marketing for treatment of symptoms secondary to BPH. The approved BPH –related indications are to relieve prostatic obstruction secondary to BPH in men at least 60 years of age, or men less than 60 years of age who are poor surgical candidates, and whose prostates are at least 2.5 cm in length. A contraindication is fracture distraction defects of the posterior urethra. The device is not intended for temporary use.

Clinical Practice Guidelines

The AUA 2003 guidelines suggests that "because prostatic stents are associated with significant complications, such as encrustation, infection and chronic pain, their placement should be considered only in high-risk patients, especially those with urinary retention."(3) The ICBPH has classified prostatic stents as acceptable with restriction since 1993.(5,19) According to the Fifth ICBPH, prostatic stents have been successfully used in patients at high risk for anesthesia-related complications or who have a short life expectancy, and the ideal patient is frail, elderly, and suffering from urinary retention.(19)

Findings

- **One retrospective study reported that fixed stents provide more symptom relief and greater improvements in peak urinary flow rates than spiral stents, TUT or TRH.**

There was one nonrandomized, unblinded, retrospective comparison (Montorsi et al., 1994)(185) among groups of 30 patients who chose a fixed stent (Urolome Wallstent, American Medical System), a spiral stent (Urologische Spirale, Uromed), TUT (Prostatron, Technomed), or TRH (Prostathermer 99D, Biodan Ltd.). All of the patients were poor surgical risks because of previous cerebrovascular accidents, myocardial infarction, coagulation disorders, or obstructive pulmonary disease. Contraindications to these treatments were considered to be a prominent median lobe, prostate or bladder cancer, calculi, neurogenic bladder, or stricture. The patients in the four groups appeared to be fairly well matched in BPH Boyarsky symptom scores and physiological measures. Stents provided better results for symptoms (statistically significant) and slightly better flow rates (not statistically significant) at 12 months. Also, the fixed stent provided significantly better flow rates and symptom scores than the spiral stent. Quality of life, adverse events, perioperative events, and retreatment rates were not reported.

- **One RCT reported that ILC plus a postoperative stent led to similar physiological outcomes and rates of adverse events as ILC alone. This trial reported that the addition of the stent allowed resumption of voiding sooner after ILC.**

A randomized comparison of ILC vs. ILC with stent(195) reported that no differences in physiological outcome measures were observed with or without the stent. Adverse event rates were similarly low for both treatment groups.

Use of a stent allowed almost twice as many patients to start voiding on the first day following the operation (81% versus 43%). With the stent, the mean for start of voiding was 1.5 days, compared to over 6 days without the stent (statistically significant).

- **One trial reported that both a fixed stent and self-expanding stent cause high rates of transient irritative symptoms. The authors did not report major treatment-efficacy related outcomes.**

One trial (randomization not reported) compared a first-generation fixed-caliber stent to a second-generation self-expanding large caliber stent.(196) Short-term irritative symptoms were the primary adverse event experienced by most patients in both the fixed and self-expanding stent groups (80% and 90%, respectively). Correct positioning of the stent was more likely to be achieved in the expanding stent group (100% versus 83% in the fixed group).

The authors did not report any outcomes relating to symptoms, physiological measures, quality of life, or retreatment. Lack of data renders it difficult to evaluate the comparative efficacy of these two types of stents.

Conclusions

Benign prostatic hyperplasia (BPH) primarily affects some middle-aged and very many elderly men. Consequently, surgical and medical treatments for BPH are some of the most common therapies administered in all of medical practice. The "gold standard" treatment for BPH is transurethral resection of the prostate (TURP). In recent years, there has been a search for less invasive alternatives that will minimize or altogether avoid some of the undesirable aspects of TURP.

A purported advantage of the minimally invasive approach to treating BPH is that such procedures have fewer side effects compared to TURP. However, the published literature of controlled trials does not report adverse event rates uniformly and comprehensively when comparing minimally invasive procedures to TURP. Because some of these procedures do not appear to be as effective as TURP in relieving symptoms (see bullets, below), a clear advantage in the incidence of adverse events would be essential in order to recommend such procedures.

- Standard surgical alternatives to TURP include transurethral electrovaporization techniques (TUEVP and TUVRP), open prostatectomy, and transurethral incision of the prostate (TUIP).
- Because electrovaporization involves skills and devices similar to those used in TURP, it can be considered a modification of TURP. Symptoms and peak urinary flow rates are similar after TUEVP, TUVRP and TURP. Quality of life is also similar after TUEVP and TURP. Both hospitalization time and catheterization time are shorter for TUEVP.
- There are no current direct comparisons of open prostatectomy to TURP. Open prostatectomy and TURP are now used on different patient populations. Open prostatectomy is the preferred treatment approach for men with large prostates.
- TUIP is recommended for men with small prostates. TUIP and TURP provide similar symptom relief. TUIP results in lower retrograde ejaculation rates and shorter operation times, as well as shorter catheterization times and hospital stays than TURP. However, TURP results in higher peak urinary flow rates than TUIP.
- CLAP and TURP resulted in similar improvements in physiological measures. CLAP and TURP provided similar symptom relief and similar quality of life improvements in most trials, but one double-blinded RCT found these outcomes to be less improved after CLAP than after TURP. CLAP results in less blood loss than TURP.
- One year after surgery, symptoms and quality of life improvements are similar after VLAP and TURP. VLAP requires shorter hospitalizations and longer catheterization times than TURP. Two trials report that major adverse events are less likely after VLAP than after TURP. Three trials report that patients who receive VLAP are more likely to require retreatment than patients who receive TURP.

- One controlled trial reported that symptoms and physiological measures improve to a similar degree after HoLAP and TURP. This RCT also reported that HoLAP operations take longer than TURP operations.
- One trial reported that HoLRP and TURP improve symptoms to a similar degree and that HoLRP operations take longer than TURP operations. However, HoLRP requires a shorter length of stay and catheterization time than TURP.
- Two trials reported that after six months, HoLEP and open prostatectomy yield similar symptom improvement in patients with large prostates. Two trials reported that HoLEP required shorter hospital stays and one trial reported that HoLEP required shorter catheterization times.
- ILC and TURP generally provide similar improvements in symptoms and quality of life. Results for physiological measures were mixed. Two trials reported higher retreatment rates after ILC. Unlike TURP, ILC may not require any hospitalization time, but this may be offset by a longer catheterization time.
- Hybrid laser techniques are too varied to permit general conclusions about this category of treatment for BPH.
- RFNA results in less symptom and physiological improvement than TURP up to 24 months after treatment, and two trials reported that the two treatments have similar effects on quality of life. One trial reported that decreased ejaculate and retrograde ejaculation occur less often after RFNA than after TURP.
- Only one study examined HIFU, but it was not randomized, and patients in its groups were not comparable.
- Cooling TUMT leads to improved symptoms and physiological measures up to 12 months after treatment. Most trials report that cooling TUMT provides less symptom relief and less improvement in physiological measures than does TURP. One trial reported that retrograde ejaculation was less common after TUMT than after TURP. Retreatment rates may be higher after cooling TUMT than after TURP.
- One RCT reported that non-cooling TUMT may improve symptoms but has associated adverse events. One RCT reported that non-cooling TUMT and TURP yield similar improvements in symptoms and physiological measures, and each has different adverse events.
- One retrospective study reported that fixed stents provide more symptom relief and greater improvements in peak urinary flow rates than spiral stents, TUT or TRH.
- Transrectal hyperthermia, transurethral thermotherapy, balloon dilation, and TULIP are outdated technologies not currently recommended by any professional organization.
- Ethanol ablations, photoselective vaporization of the prostate and water-induced thermotherapy are emerging therapies not yet studied in controlled trials.

The purpose of newer treatments for BPH is to approximate the efficacy of TURP and the other standard surgeries while decreasing the potential harms associated with the standard surgeries. Some of the less invasive treatments do appear to have fewer and/or less severe immediate complications and side effects, and symptom relief approaches that of TURP. Retreatment rates suggest that symptom relief may not be as long lasting as with TURP. However, the published controlled trials are mostly small and short-term, and few of them completely reported the retreatment rates (particularly the need for TURP), adverse events and harms. Long-term effects of these treatments are currently unknown. Hence, it is presently difficult to definitively determine their place within the armamentarium of BPH treatments.

References

1. Holtgrewe HL, Mebust WK, Dowd JB, Cockett AT, Peters PC, Proctor C. Transurethral prostatectomy: practice aspects of the dominant operation in American urology. J Urol 1989 Feb;141(2):248-53.

2. Holtgrewe HL. Transurethral prostatectomy. Urol Clin North Am 1995 May;22(2):357-68.

3. Roehrborn CG, McConnell JD, Barry MJ, Benaim EA, Blute ML, Bruskewitz R, Holtgrewe HL, Kaplan SA, Lange JL, Lowe FC, Roberts RG, Stein B. AUA guideline on the management of benign prostatic hyperplasia. American Urological Association Education and Research, Inc. 2003. Available: http://www.auanet.org/timssnet/products/guidelines/bph_management.cfm.

4. Warwick RT. A urodynamic review of bladder outlet obstruction in the male and its clinical implications. Urol Clin North Am 1979 Feb;6(1):171-92.

5. Chatelain C, Denis L, Foo KT, Khoury S, McConnell J, Abrams P, Barry M, Bartsch G, Boyle P, Brawer M, Corriere J, Debruyne F, Dreikorn K, Jardin A, Lee C, Naslund M, Nordling J, Resnick M, Roehrborn C. Recommendations of the International Scientific Committee: evaluation and treatment of lower urinary tract symptoms (LUTS) in older men. In: Proceedings of the fifth international consultation on BPH. Plymouth (UK): Health Publication Ltd.; 2001. p. 519-34.

6. Stoevelaar HJ, McDonnell J. Changing therapeutic regimens in benign prostatic hyperplasia. Clinical and economic considerations. Pharmacoeconomics 2001;19(2):131-53.

7. Fitzpatrick JM, Kasidas GP, Rose GA. Hyperoxaluria following glycine irrigation for transurethral prostatectomy. Br J Urol 1981 Jun;53(3):250-2.

8. Hoekstra PT, Kahnoski R, McCamish MA, Bergen W, Heetderks DR. Transurethral prostatic resection syndrome--a new perspective: encephalopathy with associated hyperammonemia. J Urol 1983 Oct;130(4):704-7.

9. Norlen H, Dimberg M, Allgen LG, Vinnars E. Water and electrolytes in muscle tissue and free amino acids in muscle and plasma in connection with transurethral resection of the prostate. II. Isotonic 2.2% glycine solution as an irrigating fluid. Scand J Urol Nephrol 1990;24(2):95-101.

10. Dimberg M, Norlen H, Allgen LG, Allgen T, Wallin M. A comparison between two hypotonic irrigating solutions used in transurethral resections of the prostate: sorbitol (2%)-mannitol (1%) and 1.5% glycine solutions. Scand J Urol Nephrol 1992;26(3):241-7.

11. Olsson J, Nilsson A, Hahn RG. Symptoms of the transurethral resection syndrome using glycine as the irrigant. J Urol 1995 Jul;154(1):123-8.

12. Hahn RG, Nilsson A, Farahmand BY, Ekengren J, Persson PG. Operative factors and the long-term incidence of acute myocardial infarction after transurethral resection of the prostate. Epidemiology 1996 Jan;7(1):93-5.

13. Mebust WK, Holtgrewe HL, Cockett AT, Peters PC. Transurethral prostatectomy: immediate and postoperative complications. A cooperative study of 13 participating institutions evaluating 3,885 patients. J Urol 1989 Feb;141(2):243-7.

14. Horninger W, Unterlechner H, Strasser H, Bartsch G. Transurethral prostatectomy: mortality and morbidity. Prostate 1996 Mar;28(3):195-200.

15. Donnelly V, Foran A, Murphy J, McParland P, Keane D, O'Herlihy C. Neonatal brachial plexus palsy: an unpredictable injury. Am J Obstet Gynecol 2002 Nov;187(5):1209-12.

16. Madersbacher S, Marberger M. Is transurethral resection of the prostate still justified? BJU Int 1999 Feb;83(3):227-37.

17. Madersbacher S, Djavan B, Marberger M. Minimally invasive treatment for benign prostatic hyperplasia. Curr Opin Urol 1998;8:17-26.

18. Gilling PJ, Mackey M, Cresswell M, Kennett K, Kabalin JN, Fraundorfer MR. Holmium laser versus transurethral resection of the prostate: a randomized prospective trial with 1-year followup. J Urol 1999 Nov;162(5):1640-4.

19. Debruyne FM, Djavan B, De la Rosette J, Desgrandchamps F, Fourcade R, Gibbon R, Kaplan S, Hartung R, Krane R, Manyak M, Mebust W, Muschter R, Murai M, Schulman CC, Sedelaar JP, Stein B, Teillac P, Zlotta A. Interventional therapy for benign prostatic hyperplasia. In: Proceedings of the fifth international consultation on BPH. Plymouth (UK): Health Publication Ltd.; 2001. p. 399-421.

20. Barry MJ, Fowler FJ Jr, O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK, Cockett AT. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. J Urol 1992 Nov;148(5):1549-57; discussion 1564.

21. Madsen PO, Iversen P. A point system for selecting operative candidates. In: Hinman F Jr, editors. Benign prostatic hypertrophy. New York: Springer-Verlag; 1983. p. 763-5.

22. Ackerman SJ, Rein AL, Blute M, Beusterien K, Sullivan EM, Tanio CP, Manyak MJ, Strauss MJ. Cost effectiveness of microwave thermotherapy in patients with benign prostatic hyperplasia: part I-methods. Urology 2000 Dec 20;56(6):972-80.

23. Schulz MW, Chen J, Woo HH, Keech M, Watson ME, Davey PJ. A comparison of techniques for eliciting patient preferences in patients with benign prostatic hyperplasia. J Urol 2002 Jul;168(1):155-9.

24. Sech SM, Montoya JD, Bernier PA, Barnboym E, Brown S, Gregory A, Roehrborn CG. The so-called 'placebo effect' in benign prostatic hyperplasia treatment trials represents partially a conditional regression to the mean induced by censoring. Urology 1998;51:242-50.

25. D'Agostino RB Sr. Non-inferiority trials: advances in concepts and methodology. Stat Med 2003 Jan;22(2):165-7.

26. D'Agostino RB Sr, Massaro JM, Sullivan LM. Non-inferiority trials: design concepts and issues - the encounters of academic consultants in statistics. Stat Med 2003 Jan;22(2):169-86.

27. O'Mallry AJ, Normand ST, Kuntz RE. Application of models for multivariate mixed outcomes to medical device trials: coronary artery stenting. Stat Med 2003 Jan;22(2):313-36.

28. Cooper EC. Methodological issues in AIDS clinical trials. Active control equivalence trials. J Acquir Immune Defic Syndr 1990;3 Suppl 2:S77-81.

29. Meeting transcript. Cardiovascular and Renal Drugs Advisory Committee 82nd Meeting. 1997 Oct 23; Bethesda (MD). Rockville (MD): U.S. Food and Drug Administration; 1997 Oct 23. 161 p. Also available: http://www.fda.gov/ohrms/dockets/ac/97/transcpt/3338t1.pdf.

30. Office of Science Coordination and Communication. Guidance for institutional review boards and clinical investigators. Drugs and biologics. [Internet]. Rockville (MD): U.S. Food and Drug Administration; 1998 Sep [cited 2003 Aug 19]. [11 p]. Available: http://www.fda.gov/oc/ohrt/irbs/drugsbiologics.html.

31. Hung HM, Wang SJ, Tsong Y, Lawrence J, O'Neil RT. Some fundamental issues with non-inferiority testing in active controlled trials. Stat Med 2003 Jan;22(2):213-25.

32. Wang SJ, Hung HM. TACT method for non-inferiority testing in active controlled trials. Stat Med 2003 Jan;22(2):227-38.

33. Rothmann M, Li N, Chen G, Chi GY, Temple R, Tsoi HH. Design and analysis of non-inferiority mortality trials in oncology. Stat Med 2003 Jan;22(2):239-64.

34. Greene WL, Concato J, Feinstein AR. Claims of equivalence in medical research: are they suppored by the evidence. Ann Intern Med 2000 May;132(9):715-22.

35. Vuorinen J. A practical approach for the assessment of bioequivalence under selected higher-order cross-over designs. Stat Med 1997 Oct 15;16(19):2229-43.

36. Makuch R, Johnson M. Issues in planning and interpreting active control equivalence studies. J Clin Epidemiol 1989;42(6):503-11.

37. Haines SJ, Walters BC. Proof of equivalence. The inference of statistical significance. Caveat emptor [editorial]. Neurosurgery 1993 Sep;33(3):432-3.

38. Djavan B. Benign prostatic hyperplasia: where do we stand in the new millennium? Curr Opin Urol 2002;12:1-2.

39. Littlejohn JO Jr, Ghafar MA, Kang YM, Kaplan SA. Transurethral resection of the prostate: the new old standard. Curr Opin Urol 2002 Jan;12(1):19-23.

40. May F, Guenther M, Fastenmeier K, Hartung R. Improved high-frequency surgery for transurethral resection of the prostate: report from a multicenter trial and identification of risk groups [abstract ID: 101757]. In: 2003 AUA annual meeting; 2003 Apr 26-May 1; Chicago (IL). Baltimore (MD): American Urological Association; 2003. Also available: http://aua03.agora.com/planner/displayabstract.asp?presentationid=1729.

41. Tucker RD, Sievert CE, Kramolowsky EV, Vennes JA, Silvis SE. The interaction between electrosurgical generators, endoscopic electrodes, and tissue. Gastrointest Endosc 1992 Mar-Apr;38(2):118-22.

42. Grundy PL, Budd DW, England R. A randomized controlled trial evaluating the use of sterile water as an irrigation fluid during transurethral electrovaporization of the prostate. Br J Urol 1997 Dec;80(6):894-7.

43. Kursh ED, Concepcion R, Chan S, Hudson P, Ratner M, Eyre R. Interstitial laser coagulation versus transurethral prostate resection for treating benign prostatic obstruction: a randomized trial with 2-year follow-up. Urology 2003 Mar;61(3):573-8.

44. Cetinkaya M, Ulusoy E, Ozturk B, Inal G, Memis A, Akdemir O. Transurethral resection or electrovaporization in the treatment of BPH. Br J Urol 1998 Apr;81(4):652-4.

45. Borboroglu PG, Kane CJ, Ward JF, Roberts JL, Sands JP. Immediate and postoperative complications of transurethral prostatectomy in the 1990s. J Urol 1999 Oct;162(4):1307-10.

46. Meyhoff HH. Transurethral versus transvesical prostatectomy. Clinical, urodynamic, renographic and economic aspects. A randomized study. Scand J Urol Nephrol Suppl 1987;102:1-26.

47. Deckert T, Yokoyama H, Mathiesen E, Ronn B, Jensen T, Feldt-Rasmussen B, Borch-Johnsen K, Jensen JS. Cohort study of predictive value of urinary albumin excretion for atherosclerotic vascular disease in patients with insulin dependent diabetes. BMJ 1996 Apr 6;312(7035):871-4.

48. Proceedings of the fifth international consultation on BPH. Plymouth (UK): Health Publication Ltd.; 2001. 535 p.

49. de la Rosette JJ, Alivizatos G, Madersbacher S, Perachino M, Thomas D, Desgrandchamps F, de Wildt M. EAU Guidelines on benign prostatic hyperplasia (BPH). Eur Urol 2001 Sep;40(3):256-63; discussion 264.

50. Kaplan SA, Laor E, Fatal M, Te AE. Transurethral resection of the prostate versus transurethral electrovaporization of the prostate: a blinded, prospective comparative study with 1-year followup. J Urol 1998 Feb;159(2):454-8.

51. Netto NR Jr, De Lima ML, Lucena R, Lavoura NS, Cortado PL, Netto MR. Is transurethral vaporization a remake of transurethral resection of the prostate. J Endourol 1999 Oct;13(8):591-4.

52. Hammadeh MY, Madaan S, Singh M, Philp T. Two-year follow-up of a prospective randomised trial of electrovaporization versus resection of prostate. Eur Urol 1998 Sep;34(3):188-92.

53. Cabelin MA, Te AE, Kaplan SA. Transurethral vaporization of the prostate: current techniques. Curr Urol Rep 2000 Jul;1(2):116-23.

54. van Swol CF, van Vliet RJ, Verdaasdonk RM, Boon TA. Electrovaporization as a treatment modality for transurethral resection of the prostate: influence of generator type. Urology 1999 Feb;53(2):317-21.

55. Talic RF, El Tiraifi A, El Faqih SR, Hassan SH, Attassi RA, Abdel-Halim RE. Prospective randomized study of transurethral vaporization resection of the prostate using the thick loop and standard transurethral prostatectomy. Urology 2000 Jun;55(6):886-90; discussion 890-1.

56. American Urological Association, AUA BPH Guideline Update Panel. Management of BPH (2003). Baltimore (MD): American Urological Association Education and Research, Inc.; 2003. 315 p. Also available: http://shop.auanet.org/timssnet/products/guidelines/bph_management.cfm.

57. Helke C, Manseck A, Hakenberg OW, Wirth MP. Is transurethral vaporesection of the prostate better than standard transurethral resection. Eur Urol 2001 May;39(5):551-7.

58. Kupeli S, Yilmaz E, Soygur T, Budak M. Randomized study of transurethral resection of the prostate and combined transurethral resection and vaporization of the prostate as a therapeutic alternative in men with benign prostatic hyperplasia. J Endourol 2001 Apr;15(3):317-21.

59. Cetinkaya M, Ozturk B, Akdemir O, Aki FT. A comparison of fluid absorption during transurethral resection and transurethral vaporization for benign prostatic hyperplasia. BJU Int 2000 Nov;86(7):820-3.

60. Ekengren J, Haendler L, Hahn RG. Clinical outcome 1 year after transurethral vaporization and resection of the prostate. Urology 2000 Feb;55(2):231-5.

61. Hammadeh MY, Madaan S, Singh M, Philp T. A 3-year follow-up of a prospective randomized trial comparing transurethral electrovaporization of the prostate with standard transurethral prostatectomy. BJU Int 2000 Oct;86(6):648-51.

62. Hammadeh MY, Fowlis GA, Singh M, Philp T. Transurethral electrovaporization of the prostate--a possible alternative to transurethral resection: a one-year follow-up of a prospective randomized trial. Br J Urol 1998 May;81(5):721-5.

63. Schatzl G, Madersbacher S, Djavan B, Lang T, Marberger M. Two-year results of transurethral resection of the prostate versus four 'less invasive' treatment options. Eur Urol 2000 Jun;37(6):695-701.

64. Schatzl G, Madersbacher S, Lang T, Marberger M. The early postoperative morbidity of transurethral resection of the prostate and of 4 minimally invasive treatment alternatives. J Urol 1997 Jul;158(1):105-10; 110-1.

65. Erdagi U, Akman RY, Sargin SY, Yazicioglu A. Transurethral electrovaporization of the prostate versus transurethral resection of the prostate: a prospective randomized study. Arch Ital Urol Androl 1999 Jun;71(3):125-30.

66. Gotoh M, Okamura K, Hattori R, Nishiyama N, Kobayashi H, Tanaka K, Yamada S, Kato T, Kinukawa T, Ono Y, Ohshima S. A randomized comparative study of the Bandloop versus the standard loop for transurethral resection of the prostate. J Urol 1999 Nov;162(5):1645-7.

67. Cetinkaya M, Ulusoy E, Adsan O, Saglam H, Ozturk B, Basay S. Comparative early results of transurethral electroresection and transurethral electrovaporization in benign prostatic hyperplasia. Br J Urol 1996 Dec;78(6):901-3.

68. Gallucci M, Puppo P, Perachino M, Fortunato P, Muto G, Breda G, Mandressi A, Comeri G, Boccafoschi C, Francesca F, Guazzieri S, Pappagallo GL. Transurethral electrovaporization of the prostate vs. transurethral resection. Results of a multicentric, randomized clinical study on 150 patients. Eur Urol 1998;33(4):359-64.

69. Kupeli B, Yalcinkaya F, Topaloglu H, Karabacak O, Gunlusoy B, Unal S. Efficacy of transurethral electrovaporization of the prostate with respect to standard transurethral resection. J Endourol 1998 Dec;12(6):591-4.

70. Shokeir AA, al-Sisi H, Farage YM, el-Maaboud MA, Saeed M, Mutabagani H. Transurethral prostatectomy: a prospective randomized study of conventional resection and electrovaporization in benign prostatic hyperplasia. Br J Urol 1997 Oct;80(4):570-4.

71. Van Melick HH, Van Venrooij GE, Eckhardt MD, Boon TA. A randomized controlled trial comparing transurethral resection of the prostate, contact laser prostatectomy and electrovaporization in men with benign prostatic hyperplasia: urodynamic effects. J Urol 2002 Sep;168(3):1058-62.

72. Meyhoff HH, Nordling J, Hald T. Urodynamic evaluation of transurethral versus transvesical prostatectomy. A randomized study. Scand J Urol Nephrol 1984;18(1):27-35.

73. Orandi A. Transurethral incision of prostate compared with transurethral resection of prostate in 132 matching cases. J Urol 1987 Oct;138(4):810-5.

74. Saporta L, Aridogan IA, Erlich N, Yachia D. Objective and subjective comparison of transurethral resection, transurethral incision and balloon dilatation of the prostate. A prospective study. Eur Urol 1996;29(4):439-45.

75. Riehmann M, Knes JM, Heisey D, Madsen PO, Bruskewitz RC. Transurethral resection versus incision of the prostate: a randomized, prospective study. Urology 1995 May;45(5):768-75.

76. Jahnson S, Dalen M, Gustavsson G, Pedersen J. Transurethral incision versus resection of the prostate for small to medium benign prostatic hyperplasia. Br J Urol 1998 Feb;81(2):276-81.

77. Dorflinger T, Jensen FS, Krarup T, Walter S. Transurethral prostatectomy compared with incision of the prostate in the treatment of prostatism caused by small benign prostate glands. Scand J Urol Nephrol 1992;26(4):333-8.

78. Dorflinger T, Oster M, Larsen JF, Walter S, Krarup T. Transurethral prostatectomy or incision of the prostate in the treatment of prostatism caused by small benign prostates. Scand J Urol Nephrol Suppl 1987;104:77-81.

79. Soonawalla PF, Pardanani DS. Transurethral incision versus transurethral resection of the prostate. A subjective and objective analysis. Br J Urol 1992 Aug;70(2):174-7.

80. Christensen MM, Aagaard J, Madsen PO. Transurethral resection versus transurethral incision of the prostate. A prospective randomized study. Urol Clin North Am 1990 Aug;17(3):621-30.

81. Larsen EH, Dorflinger T, Gasser C, Graversen PH, Bruskewitz RC. Transurethral incision versus transurethral resection of the prostate for treatment of benign prostatic hypertrophy, a preliminary report. Scand J Urol Nephrol 1987;21(suppl 104):83-6.

82. D'Ancona CA, Netto NR Junior, Cara AM, Ikari O. Internal urethrotomy of the prostatic urethra or transurethral resection in benign prostatic hyperplasia. J Urol 1990 Oct;144(4):918-20.

83. Nielsen HO. Transurethral prostatotomy versus tranurethral prostatectomy in benign prostatic hypertrophy. A prospective randomized study. Br J Urol 1988;61:435-8.

84. Li MK, Ng AS. Bladder neck resection and transurethral resection of the prostate: a randomized prospective trial. J Urol 1987 Oct;138(4):807-9.

85. Hellstrom P, Lukkarinen O, Kontturi M. Bladder neck incision or transurethral electroresection for the treatment of urinary obstruction caused by a small benign prostate? A randomized urodynamic study. Scand J Urol Nephrol 1986;20(3):187-92.

86. Kitagawa M, Furuse H, Fukuta K, Aso Y. Holmium:YAG laser resection of the prostate versus visual laser ablation of the prostate and transurethral ultrasound-guided laser induced prostatectomy: a retrospective comparative study. Int J Urol 1998 Mar;5(2):152-6.

87. Keoghane SR, Cranston DW, Lawrence KC, Doll HA, Fellows GJ, Smith JC. The Oxford Laser Prostate Trial: a double-blind randomized controlled trial of contact vaporization of the prostate against transurethral resection; preliminary results. Br J Urol 1996 Mar;77(3):382-5.

88. U.S. Food and Drug Administration, Center for Devices and Radiological Health. 510(k) summary of safety and effectiveness. SLT CL MD contact laser system and delivery fibers. K972548. Rockville (MD): U.S. Food and Drug Administration, Center for Devices and Radiological Health; 1998 Apr 28. 4 p. Also available: http://www.fda.gov.

89. Tuhkanen K, Heino A, Ala-Opas M. Contact laser prostatectomy compared to TURP in prostatic hyperplasia smaller than 40 ml Six-month follow-up with complex urodynamic assessment. Scand J Urol Nephrol 1999 Feb;33(1):31-4.

90. Zorn BH, Bauer JJ, Ruiz HE, Thrasher JB. Randomized trial of safety and efficacy of transurethral resection of the prostate using contact laser versus electrocautery. Tech Urol 1999 Dec;5(4):198-201.

91. Keoghane SR, Lawrence KC, Gray AM, Doll HA, Hancock AM, Turner K, Sullivan ME, Dyar O, Cranston D. A double-blind randomized controlled trial and economic evaluation of transurethral resection vs contact laser vaporization for benign prostatic enlargement: a 3-year follow-up. BJU Int 2000 Jan;85(1):74-8.

92. Keoghane SR, Doll HA, Lawrence KC, Jenkinson CP, Cranston DW. The Oxford Laser Prostate Trial: sexual function data from a randomized controlled clinical trial of contact laser prostatectomy. Eur Urol 1996;30(4):424-8.

93. Jenkinson C, Gray A, Doll H, Lawrence K, Keoghane S, Layte R. Evaluation of index and profile measures of health status in a randomized controlled trial. Comparison of the medical outcomes study 36-item short form health survey, EuroQol, and disease specific measures. Med Care 1997 Nov;35(11):1109-18.

94. Keoghane SR, Lawrence KC, Jenkinson CP, Doll HA, Chappel DB, Cranston DW. The Oxford Laser Prostate Trial: sensitivity to change of three measures of outcome. Urology 1996 Jan;47(1):43-7.

95. Suvakovic N, Hindmarsh JR. A step towards day case prostatectomy. Br J Urol 1996 Feb;77(2):212-4.

96. Cowles RS 3d, Kabalin JN, Childs S, Lepor H, Dixon C, Stein B, Zabbo A. A prospective randomized comparison of transurethral resection to visual laser ablation of the prostate for the treatment of benign prostatic hyperplasia. Urology 1995 Aug;46(2):155-60.

97. Jung P, Mattelaer P, Wolff JM, Mersdorf A, Jakse G. Visual laser ablation of the prostate: efficacy evaluated by urodynamics and compared to TURP. Eur Urol 1996;30(4):418-23.

98. Costello AJ, Crowe HR, Jackson T, Street A. A randomised single institution study comparing laser prostatectomy and transurethral resection of the prostate. Ann Acad Med Singapore 1995 Sep;24(5):700-4.

99. Anson K, Nawrocki J, Buckley J, Fowler C, Kirby R, Lawrence W, Paterson P, Watson G. A multicenter, randomized, prospective study of endoscopic laser ablation versus transurethral resection of the prostate. Urology 1995 Sep;46(3):305-10.

100. Donovan JL, Peters TJ, Neal DE, Brookes ST, Gujral S, Chacko KN, Wright M, Kennedy LG, Abrams P. A randomized trial comparing transurethral resection of the prostate, laser therapy and conservative treatment of men with symptoms associated with benign prostatic enlargement: The CLasP study. J Urol 2000 Jul;164(1):65-70.

101. Gujral S, Abrams P, Donovan JL, Neal DE, Brookes ST, Chacko KN, Wright MJ, Timoney AG, Peters TJ. A prospective randomized trial comparing transurethral resection of the prostate and laser therapy in men with chronic urinary retention: The CLasP study. J Urol 2000 Jul;164(1):59-64.

102. Chacko KN, Donovan JL, Abrams P, Peters TJ, Brookes ST, Thorpe AC, Gujral S, Wright M, Kennedy LG, Neal DE. Transurethral prostatic resection or laser therapy for men with acute urinary retention: the CLasP randomized trial. J Urol 2001;166(1):166-70.

103. Sengor F, Kose O, Yucebas E, Beysel M, Erdogan K, Narter F. A comparative study of laser ablation and transurethral electroresection for benign prostatic hyperplasia: results of a 6-month follow-up [published erratum appears in Br J Urol 1997 Feb;79(2):304]. Br J Urol 1996 Sep;78(3):398-400.

104. Brookes ST, Donovan JL, Peters TJ, Abrams P, Neal DE. Sexual dysfunction in men after treatment for lower urinary tract symptoms: evidence from randomised controlled trial. BMJ 2002 May 4;324(7345):1059-61.

105. Noble SM, Coast J, Brookes S, Neal DE, Abrams P, Peters TJ, Donovan JL. Transurethral prostate resection, noncontact laser therapy or conservative management in men with symptoms of benign prostatic enlargement? An economic evaluation. J Urol 2002 Dec 01;168(6):2476-82.

106. Kabalin JN. Laser prostatectomy performed with a right angle firing neodymium:YAG laser fiber at 40 watts power setting. J Urol 1993 Jul;150(1):95-9.

107. Boon TA, Lepor H, Muschter R, McCullough DL. Laser treatment of benign prostatic hyperplasia (BPH) workshop. Prog Clin Biol Res 1994;386:535-44.

108. Kabalin JN, Gill HS, Bite G, Wolfe V. Comparative study of laser versus electrocautery prostatic resection: 18-month followup with complex urodynamic assessment. J Urol 1995 Jan;153(1):94-7; discussion 97-8.

109. Shingleton WB, Farabaugh P, May W. Three-year follow-up of laser prostatectomy versus transurethral resection of the prostate in men with benign prostatic hyperplasia. Urology 2002 Aug;60(2):305-8.

110. Bryan NP, Hastie KJ, Chapple CR. Randomised prospective trial of contact laser prostatectomy (CLAP) versus visual laser coagulation of the prostate (VLAP) for the treatment of benign prostatic hyperplasia. 2-year follow-up. Eur Urol 2000 Sep;38(3):265-71.

111. Narayan P, Tewari A, Aboseif S, Evans C. A randomized study comparing visual laser ablation and transurethral evaporation of prostate in the management of benign prostatic hyperplasia. J Urol 1995 Dec;154(6):2083-8.

112. Beerlage HP, Francisca EA, d'Ancona FC, Debruyne FM, De la Rosette JJ. Urolase v ultraline fibers in laser prostatectomy: 3-year follow-up of a randomized study. J Endourol 1998 Dec;12(6):575-80.

113. de la Rosette JJ, te Slaa E, de Wildt MJ, Debruyne FM. Experience with the Ultraline and Urolase laser fibers: is there any difference. World J Urol 1995;13(2):98-103.

114. de la Rosette J. Laser therapy: to combine the best of the new with the best of the old. J Urol (Paris) 1995;101(1):37-9.

115. Tan AH, Gilling PJ. Holmium laser prostatectomy: current techniques. Urology 2002 Jul;60(1):152-6.

116. Paterson RF, Lingeman JE. Holmium laser prostatectomy. Curr Urol Rep 2001 Aug;2(4):269-76.

117. Hettiarachchi JA, Samadi AA, Konno S, Das AK. Holmium laser enucleation for large (greater than 100 mL) prostate glands. Int J Urol 2002 May;9(5):233-6.

118. CDRH 510(k) database search. [internet]. Rockville (MD): U.S. Food and Drug Administration (FDA), Center for Devices and Radiological Health (CDRH); [updated 2003 Sep 05]; [cited 2003 Sep 08]. Available: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm.

119. Mottet N, Anidjar M, Bourdon O, Louis JF, Teillac P, Costa P, Le Duc A. Randomized comparison of transurethral electroresection and Holmium:YAG laser vaporization for symptomatic benign prostatic hyperplasia. J Endourol 1999 Mar;13(2):127-30.

120. Gilling PJ, Cass CB, Malcolm A, Cresswell M, Fraundorfer MR, Kabalin JN. Holmium laser resection of the prostate versus neodymium:yttrium-aluminum-garnet visual laser ablation of the prostate: a randomized prospective comparison of two techniques for laser prostatectomy. Urology 1998 Apr;51(4):573-7.

121. Fraundorfer MR, Gilling PJ, Kennett KM, Dunton NG. Holmium laser resection of the prostate is more cost effective than transurethral resection of the prostate: results of a randomized prospective study. Urology 2001 Mar;57(3):454-8.

122. Gilling PJ, Kennett KM, Fraundorfer MR. Holmium laser resection v transurethral resection of the prostate: results of a randomized trial with 2 years of follow-up. J Endourol 2000 Nov;14(9):757-60.

123. Kuntz RM, Lehrich K. Transurethral holmium laser enucleation versus transvesical open enucleation for prostate adenoma greater than 100 gm.: a randomized prospective trial of 120 patients. J Urol 2002 Oct;168(4 Pt 1):1465-9.

124. Moody JA, Lingeman JE. Holmium laser enucleation for prostate adenoma greater than 100 gm.: comparison to open prostatectomy. J Urol 2001 Feb;165(2):459-62.

125. Perlmutter AP, Muschter R. Interstitial laser prostatectomy. Mayo Clin Proc 1998 Sep;73(9):903-7.

126. Muschter R. Interstitial laser therapy. Curr Opin Urol 1996;6:33-8.

127. Pypno W, Husiatynski W. Treatment of a benign prostatic hyperplasia by Nd:YAG laser – own experience. Eur Urol 2000 Aug;38(2):194-8.

128. Martenson AC, De la Rosette JJMCH. Interstitial laser coagulation in the treatment of benign prostatic hyperplasia using a diode laser system: results of an evolving technology. Prostate Cancer Prostatic Dis 1999;2(3):148-54.

129. Norby B, Nielsen HV, Frimodt-Moller PC. Transurethral interstitial laser coagulation of the prostate and transurethral microwave thermotherapy vs transurethral resection or incision of the prostate: results of a randomized, controlled study in patients with symptomatic benign prostatic [tr. BJU Int 2002 Dec;90(9):853-62.

130. Arai Y, Aoki Y, Okubo K, Maeda H, Terada N, Matsuta Y, Maekawa S, Ogura K. Impact of interventional therapy for benign prostatic hyperplasia on quality of life and sexual function: a prospective study. J Urol 2000 Oct;164(4):1206-11.

131. Fenter TC. (American Urological Association). Personal communication. 2004 Mar 4.

132. Shingleton WB, Terrell F, Renfroe DL, Kolski JM, Fowler JE Jr. A randomized prospective study of laser ablation of the prostate versus transurethral resection of the prostate in men with benign prostatic hyperplasia. Urology 1999 Dec;54(6):1017-21.

133. Tuhkanen K, Heino A, Ala-Opas M. Two-year follow-up results of a prospective randomized trial comparing hybrid laser prostatectomy with TURP in the treatment of big benign prostates. Scand J Urol Nephrol 2001 Jun;35(3):200-4.

134. Tuhkanen K, Heino A, Alaopas M. Hybrid laser treatment compared with transurethral resection of the prostate for symptomatic bladder outlet obstruction caused by a large benign prostate: a prospective, randomized trial with a 6-month follow-up. BJU Int 1999 Nov;84(7):805-9.

135. Carter A, Sells H, Speakman M, Ewings P, MacDonagh R, O'Boyle P. A prospective randomized controlled trial of hybrid laser treatment or transurethral resection of the prostate, with a 1-year follow-up. BJU Int 1999 Feb;83(3):254-9.

136. Carter A, Sells H, Speakman M, Ewings P, O'Boyle P, MacDonagh R. Quality of life changes following KTP/Nd:YAG laser treatment of the prostate and TURP. Eur Urol 1999 Aug;36(2):92-8.

137. Shingleton WB, Renfroe LD, Kolski JM, Fowler JE Jr. A randomized prospective study of transurethral electrovaporization vs laser ablation of the prostate in men with benign prostatic hypertrophy. Scand J Urol Nephrol 1998 Jul;32(4):266-9.

138. Shingleton WB, Kolski J, Renfroe DL, Fowler JE Jr. Electrovaporization of the prostate versus laser ablation of the prostate in men with benign prostatic hypertrophy: a pressure-flow analysis. Urol Int 1998 Aug;60(4):224-8.

139. Gilling PJ, Cass CB, Malcolm AR, Fraundorfer MR. Combination holmium and Nd:YAG laser ablation of the prostate: initial clinical experience. J Endourol 1995 Apr;9(2):151-3.

140. Malek RS, Hai MA, Nseyo UO, Lapeyrolerie J. Photoselective vaporization of the prostate: breakthrough treatment for BPH. Urol Times 2002 May;30(Suppl 1):4-20.

141. Giannakopoulos X, Grammeniatis E, Gartzios A, et al. Transurethral needle ablation (TUNA) of the prostate: preliminary results using the new generation TUNA III catheter on patients with symptomatic BPH controlled by a series of 50 patients using TUNA II device. Eur Urol 1996;30:986.

142. Heaton JP. Radiofrequency thermal ablation of the prostate: the TUNA technique. Tech Urol 1995 Spring;1(1):3-10.

143. Chapple CR, Issa MM, Woo H. Transurethral needle ablation (TUNA®). A critical review of radiofrequency thermal therapy in the management of benign prostatic hyperplasia. Eur Urol 1999;35(2):119-28.

144. Issa MM, Myrick SE, Symbas NP. The TUNA procedure for BPH: review of technology. Infect Urol 1998;11(4):104-11. Also available: http://www.medscape.com/SCP/IIU/1998/v11.n04/u3086.issa/pnt-u3086.issa.html.

145. Montie JE, Tremper K. Anesthesia requirements during transurethral needle ablation procedure [letter; comment]. Urology 1998 Jul;52(1):158.

146. Zlotta AR, Djavan B. Minimally invasive therapies for benign prostatic hyperplasia in the new millennium: long-term data. Curr Opin Urol 2002 Jan;12(1):7-14.

147. Bruskewitz R, Issa MM, Roehrborn CG, Naslund MJ, Perez-Marrero R, Shumaker BP, Oesterling JE. A prospective, randomized 1-year clinical trial comparing transurethral needle ablation to transurethral resection of the prostate for the treatment of symptomatic benign prostatic hyperplasia. J Urol 1998 May;159(5):1588-93; discussion 1593-4.

148. Roehrborn CG, Burkhard FC, Bruskewitz RC, Issa MM, Perez-Marrero R, Naslund MJ, Shumaker BP. The effects of transurethral needle ablation and resection of the prostate on pressure flow urodynamic parameters: analysis of the United States randomized study. J Urol 1999 Jul;162(1):92-7.

149. Mostafid AH, Harrison NW, Thomas PJ, Fletcher MS. A prospective randomized trial of interstitial radiofrequency therapy versus transurethral resection for the treatment of benign prostatic hyperplasia. Br J Urol 1997 Jul;80(1):116-22.

150. Hill B, Belville W, Bruskewitz R, Issa M, Perez-Marrero R, Roehrborn C, Terris M, Naslund M. Transurethral needle ablation versus transurethral resection of the prostate for the treatment of symptomatic benign prostatic hyperplasia: 5-year results of a prospective, randomized, multicenter clinical trial. J Urol 2004 Jun;171(6 Pt 1):2336-40.

151. Focus Surgery. Noninvasive therapy for prostate diseases: Focus surgery has positive prostate cancer results using high intensity focused ultrasound (HIFU). [internet]. Indianapolis (IN): Focus Surgery, Inc.; 2003 [cited 2003 Sep 09]. [2 p]. Available: http://www.focus-surgery.com.

152. Premarket approval (PMA) database for Urologix Targis (tm) system. P970008. [internet]. Rockville (MD): U.S. Food and Drug Administration, Center for Devices and Radiological Health (CDRH); 1999 Dec 16 [cited 2003 Sep 02]. [1 p]. Available: http://www.accessdata.fda.gov.

153. Premarket approval (PMA) database for Prostatron system, hyperthermia. P950014. [internet]. Rockville (MD): U.S. Food and Drug Administration, Center for Devices and Radiological Health (CDRH); 1999 Nov 26 [cited 2003 Sep 02]. [1 p]. Available: http://www.accessdata.fda.gov.

154. Urologix. Prostatron treatment. [internet]. Minneapolis (MN): Urologix, Inc.; 2003 [cited 2003 Aug 12]. [1 p]. Available: http://www.urologix.com.

155. Lingeman J. Thermotherapy evolves beyond cooling: the logic behind the next generation devices. [internet]. Northbrook (IL): Thermatrx; 2002 [cited 2003 Sep 02]. [2 p]. Available: http://www.thermatrx.com.

156. Larson TR, Blute ML, Tri JL, Whitlock SV. Contrasting heating patterns and efficiency of the Prostatron and Targis microwave antennae for thermal treatment of benign prostatic hyperplasia. Urology 1998 Jun;51(6):908-15.

157. Rivas DA, Bagley D, Gomella LG, Hirsch IH, Hubert C, Lombardo S, McGinnis DE, Mulholland SG, Shenot PJ, Strup SE, Vasavada SP. Transurethral microwave thermotherapy of the prostate without intravenous sedation: results of a single United States center using both low- and high-energy protocols. TJUH TUMT Study Group. Tech Urol 2000 Dec;6(4):282-7.

158. Center for Devices and Radiological Health (CDRH). FDA public health notification: serious injuries from microwave thermotherapy for benign prostatic hyperplasia. [internet]. Rockville (MD): U.S. Food and Drug Administration; 2000 Oct 11 [cited 2003 Jan 27]. [3 p]. Available: http://www.fda.gov/cdrh/safety.html.

159. Roehrborn CG, Preminger G, Newhall P, Denstedt J, Razvi H, Chin LJ, Perlmutter A, Barzell W, Whitmore W, Fritzsch R, Sanders J, Sech S, Womack S. Microwave thermotherapy for benign prostatic hyperplasia with the Dornier Urowave: results of a randomized, double-blind, multicenter, sham-controlled trial. Urology 1998 Jan;51(1):19-28.

160. Venn SN, Montgomery BS, Sheppard SA, Hughes SW, Beard RC, Bultitiude MI, Lloyd-Davies RW, Tiptaft RC. Microwave hyperthermia in benign prostatic hypertrophy: a controlled clinical trial. Br J Urol 1995 Jul;76(1):73-6.

161. Bdesha AS, Bunce CJ, Snell ME, Witherow RO. A sham controlled trial of transurethral microwave therapy with subsequent treatment of the control group. J Urol 1994 Aug;152(2 Pt 1):453-8.

162. Bdesha AS, Bunce CJ, Kelleher JP, Snell ME, Vukusic J, Witherow RO. Transurethral microwave treatment for benign prostatic hypertrophy: a randomised controlled clinical trial. BMJ 1993 May 15;306(6888):1293-6.

163. Laduc R. Thermotherapy. Results of a prospective, randomized, double blind, placebo controlled study. In: Laduc R, Weil EH, Zerbib M, Perrin P, Denis L. Thermotherapy and hyperthermia workshop. Prog Clin Biol Res 1994;386:487-98.

164. Mulvin D, Creagh T, Kelly D, Smith J, Quinlan D, Fitzpatrick J. Transurethral microwave thermotherapy versus transurethral catheter therapy for benign prostatic hyperplasia. Eur Urol 1994;26(1):6-9.

165. Perrin P. TUMT versus sham in BPH patients. In: Laduc R, Weil EH, Zerbib M, Perrin P, Denis L. Thermotherapy and hyperthermia workshop. Prog Clin Biol Res 1994;386:487-98.

166. Ogden CW, Reddy P, Johnson H, Ramsay JW, Carter SS. Sham versus transurethral microwave thermotherapy in patients with symptoms of benign prostatic bladder outflow obstruction. Lancet 1993 Jan 2;341(8836):14-7.

167. Hansen MV, Zdanowski A. The use of a simple home flow test as a quality indicator for male patients treated for lower urinary tract symptoms suggestive of bladder outlet obstruction. Eur Urol 1997;32(1):34-8.

168. Trachtenberg J, Roehrborn CG. Updated results of a randomized, double-blind, multicenter sham-controlled trial of microwave thermotherapy with the Dornier Urowave in patients with symptomatic benign prostatic hyperplasia. Urowave Investigators Group. World J Urol 1998;16(2):102-8.

169. Larson TR, Blute ML, Bruskewitz RC, Mayer RD, Ugarte RR, Utz WJ. A high-efficiency microwave thermoablation system for the treatment of benign prostatic hyperplasia: results of a randomized, sham-controlled, prospective, double-blind, multicenter clinical trial. Urology 1998 May;51(5):731-42.

170. Blute ML, Patterson DE, Segura JW, Tomera KM, Hellerstein DK. Transurethral microwave thermotherapy v sham treatment: double-blind randomized study. J Endourol 1996 Dec;10(6):565-73.

171. Francisca EA, d'Ancona FC, Hendriks JC, Kiemeney LA, Debruyne FM, de la Rosette JJ. Quality of life assessment in patients treated with lower energy thermotherapy (Prostasoft 2.0): results of a randomized transurethral microwave thermotherapy versus sham study. J Urol 1997 Nov;158(5):1839-44.

172. Nawrocki JD, Bell TJ, Lawrence WT, Ward JP. A randomized controlled trial of transurethral microwave thermotherapy. Br J Urol 79(3):389-93.

173. Francisca EA, d'Ancona FC, Meuleman EJ, Debruyne FM, de la Rosette JJ. Sexual function following high energy microwave thermotherapy: results of a randomized controlled study comparing transurethral microwave thermotherapy to transurethral prostatic resection. J Urol 1999 Feb;161(2):486-90.

174. D'Ancona FC, Francisca EA, Witjes WP, Welling L, Debruyne FM, De La Rosette JJ. Transurethral resection of the prostate vs high-energy thermotherapy of the prostate in patients with benign prostatic hyperplasia: long-term results. Br J Urol 1998 Feb;81(2):259-64.

175. Ahmed M, Bell T, Lawrence WT, Ward JP, Watson GM. Transurethral microwave thermotherapy (Prostatron version 2.5) compared with transurethral resection of the prostate for the treatment of benign prostatic hyperplasia: a randomized, controlled, parallel study. Br J Urol 1997 Feb;79(2):181-5.

176. Dahlstrand C, Walden M, Geirsson G, Pettersson S. Transurethral microwave thermotherapy versus transurethral resection for symptomatic benign prostatic obstruction: a prospective randomized study with a 2-year follow-up. Br J Urol 1995 Nov;76(5):614-8.

177. Albala DM, Turk TM, Fulmer BR, Koleski F, Andriole G, Davis BE, Eure GR, Kabalin JN, Lingeman J, Nuzzarello J, Sundaram C. Periurethral transurethral microwave thermotherapy for the treatment of benign prostatic hyperplasia: an interim 1-year safety and efficacy analysis using the thermatrx TMx-2000. Tech Urol 2000 Dec;6(4):288-93.

178. Wagrell L, Schelin S, Nordling J, Richthoff J, Magnusson B, Schain M, Larson T, Boyle E, Duelund J, Kroyer K, Ageheim H, Mattiasson A. Feedback microwave thermotherapy versus TURP for clinical BPH--a randomized controlled multicenter study. Urology 2002 Aug;60(2):292-9.

179. Djavan B, Seitz C, Roehrborn CG, Remzi M, Fakhari M, Waldert M, Basharkhah A, Planz B, Harik M, Marberger M. Targeted transurethral microwave thermotherapy versus alpha-blockade in benign prostatic hyperplasia: outcomes at 18 months. Urology 2001 Jan;57(1):66-70.

180. Floratos DL, Kiemeney LA, Rossi C, Kortmann BB, Debruyne FM, de La Rosette JJ. Long-term followup of randomized transurethral microwave thermotherapy versus transurethral prostatic resection study. J Urol 2001 May;165(5):1533-8.

181. Francisca EA, d'Ancona FC, Hendriks JC, Kiemeney LA, Debruyne FM, de La Rosette JJ. A randomized study comparing high-energy TUMT to TURP: quality-of-life results. Eur Urol 2000 Nov;38(5):569-75.

182. D'Ancona FC, Francisca EA, Witjes WP, Welling L, Debruyne FM, de la Rosette JJ. High energy thermotherapy versus transurethral resection in the treatment of benign prostatic hyperplasia: results of a prospective randomized study with 1 year of followup. J Urol 1997 Jul;158(1):120-5.

183. Zeitlin SI. Heat therapy in the treatment of prostatitis. Urology 2002 Dec;60(6 Suppl):38-40.

184. Perlmutter AP, Verdi J, Watson GM. Prostatic heat treatments for urinary outflow obstruction. J Urol 1993 Nov;150(5 Pt 2):1603-6.

185. Montorsi F, Guazzoni G, Bergamaschi F, Consonni P, Galli L, Rigatti P. A comparison of transrectal hyperthermia, transurethral thermotherapy, urolume wallstent, and prostatic spiral for benign prostatic hyperplasia patients at poor operative risk. Prostate 1994;24(3):156-61.

186. Yerushalmi A, Fishelovitz Y, Singer D, Reiner I, Arielly J, Abramovici Y, Catsenelson R, Levy E, Shani A. Localized deep microwave hyperthermia in the treatment of poor operative risk patients with benign prostatic hyperplasia. J Urol 1985 May;133(5):873-6.

187. Montorsi F, Galli L, Guazzoni G, Colombo R, Bulfamante G, Barbieri L, Matozzo V, Grazioli V, Rigatti P. Transrectal microwave hyperthermia for benign prostatic hyperplasia: long-term clinical, pathological and ultrastructural patterns. J Urol 1992 Aug;148(2 Pt 1):321-5.

188. Lindner A, Braf Z, Lev A, Golomb J, Leib Z, Siegel Y, Servadio C. Local hyperthermia of the prostate gland for the treatment of benign prostatic hypertrophy and urinary retention. Br J Urol 1990 Feb;65(2):201-3.

189. Diagnostic and therapeutic technology assessment. Endoscopic balloon dilation of the prostate. JAMA 1992 Feb 26;267(8):1123-4, 1127-8.

190. Roehrborn CG, Bartsch G, Kirby R, Andriole G, Boyle P, de la Rosette J, Perrin P, Ramsey E, Nordling J, De Campos Freire G, Arap S. Guidelines for the diagnosis and treatment of benign prostatic hyperplasia: a comparative, international overview. Urology 2001 Nov;58(5):642-50.

191. Breda G, Isgro A. Treatment of benign prostatic hyperplasia with water-induced thermotherapy: experience of a single institution. J Endourol 2002 Mar;16(2):123-6.

192. de la Rosette JJ, Alivizatos G, Laguna MP. Transurethral hot water balloon thermoablation. Curr Urol Rep 2001 Aug;2(4):302-5.

193. Ditrolio J, Patel P, Watson RA, Irwin RJ. Chemo-ablation of the prostate with dehydrated alcohol for the treatment of prostatic obstruction. J Urol 2002 May;167(5):2100-3; discussion 2103-4.

194. Lam JS, Volpe MA, Kaplan SA. Use of prostatic stents for the treatment of benign prostatic hyperplasia in high-risk patients. Curr Urol Rep 2001 Aug;2(4):277-84.

195. Petas A, Isotalo T, Talja M, Tammela TL, Valimaa T, Tormala P. A randomised study to evaluate the efficacy of a biodegradable stent in the prevention of postoperative urinary retention after interstitial laser coagulation of the prostate. Scand J Urol Nephrol 2000 Aug;34(4):262-6.

196. Yachia D, Aridogan IA. Comparison between first-generation (fixed-caliber) and second-generation (self-expanding, large caliber) temporary prostatic stents. Urol Int 1996;57(3):165-9.

197. Barry MJ. Evaluation of symptoms and quality of life in men with benign prostatic hyperplasia. Urology 2001 Dec;58(6 Suppl 1):25-32; discussion 32.

198. MacDiarmid SA, Goodson TC, Holmes TM, Martin PR, Doyle RB. An assessment of the comprehension of the American Urological Association Symptom Index. J Urol 1998 Mar;159(3):873-4.

199. Teillac P. Relief of BPO or improvement in quality of life. Eur Urol 1998;34(Suppl 2):3-9.

200. Hansen BJ, Mortensen S, Mensink HJ, Flyger H, Riehmann M, Hendolin N, Nordling J, Hald T. Comparison of the Danish Prostatic Symptom Score with the International Prostatic Symptom Score, the Madsen-Iversen and Boyarsky symptom indexes. ALFECH Study Group. Br J Urol 1998 Jan;81(1):36-41.

201. Barry MJ, Fowler FJ Jr, O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK. Correlation of the American Urological Association symptom index with self-administered versions of the Madsen-Iversen, Boyarsky and Maine Medical Assessment Program symptom indexes. Measurement Committee of the American Urological Association. J Urol 1992 Nov;148(5):1558-63; discussion 1564.

202. Barry MJ, Williford WO, Chang Y, Machi M, Jones KM, Walker-Corkery E, Lepor H. Benign prostatic hyperplasia specific health status measures in clinical research: how much change in the American Urological Association symptom index and the benign prostatic hyperplasia impact index is perceptible to patients? J Urol 1995 Nov;154(5):1770-4.

203. Hansen BJ, Flyger H, Brasso K, Schou J, Nordling J, Thorup Andersen J, Mortensen S, Meyhoff HH, Walter S, Hald T. Validation of the self-administered Danish Prostatic Symptom Score (DAN-PSS-1) system for use in benign prostatic hyperplasia. Br J Urol 1995 Oct;76(4):451-8.

204. Donovan JL, Abrams P, Peters TJ, Kay HE, Reynard J, Chapple C, De La Rosette JJ, Kondo A. The ICS-'BPH' Study: the psychometric validity and reliability of the ICSmale questionnaire. Br J Urol 1996 Apr;77(4):554-62.

205. Roehrborn CG. The placebo effect in the treatment of benign prostatic hyperplasia. In: Kirby RS, McConnell JD, Fitzpatrick JM, Roehrborn CG, Boyle P, editors. Textbook of benign prostatic hyperplasia. Oxford (UK): Isis Medical Media; 1996.

206. Boyarsky S, Jones G, Paulson DF. A new look at bladder neck obstruction by the Food and Drug Administration regulators: guidelines for investigation of benign prostatic hypertrophy. Trans Am Assoc Genitourin Surg 1977;68:29-32.

207. Donovan JL, Peters TJ, Abrams P, Brookes ST, de aa Rosette JJ, Schafer W. Scoring the short form ICSmaleSF questionnaire. International Continence Society. J Urol 2000 Dec;164(6):1948-55.

208. Bolognese JA, Kozloff RC, Kunitz SC, Grino PB, Patrick DL, Stoner E. Validation of a symptoms questionnaire for benign prostatic hyperplasia. Prostate 1992;21(3):247-54.

209. Fowler FJ Jr, Wennberg JE, Timothy RP, Barry MJ, Mulley AG Jr, Hanley D. Symptom status and quality of life following prostatectomy. JAMA 1988 May 27;259(20):3018-22.

210. Barry MJ, Cockett AT, Holtgrewe HL, McConnell JD, Sihelnik SA, Winfield HN. Relationship of symptoms of prostatism to commonly used physiological and anatomical measures of the severity of benign prostatic hyperplasia. J Urol 1993 Aug 1;150(2):351-358.

211. van Venrooij GE, Boon TA. The value of symptom score, quality of life score, maximal urinary flow rate, residual volume and prostate size for the diagnosis of obstructive benign prostatic hyperplasia: a urodynamic analysis. J Urol 1996 Jun;155(6):2014-8.

212. Bosch JL, Hop WC, Kirkels WJ, Schroder FH. The International Prostate Symptom Score in a community-based sample of men between 55 and 74 years of age: prevalence and correlation of symptoms with age, prostate volume, flow rate and residual urine volume. Br J Urol 1995 May;75(5):622-30.

213. Simpson RJ, Fisher W, Lee AJ, Russell EB, Garraway M. Benign prostatic hyperplasia in an unselected community-based population: a survey of urinary symptoms, bothersomeness and prostatic enlargement. Br J Urol 1996 Feb;77(2):186-91.

214. Roberts RO, Jacobsen SJ, Jacobson DJ, Rhodes T, Girman CJ, Lieber MM. Longitudinal changes in peak urinary flow rates in a community based cohort. J Urol 2000 Jan;163(1):107-13.

215. Sarma AV, Jacobsen SJ, Girman CJ, Jacobson DJ, Roberts RO, Rhodes T, Lieber M. Concomitant longitudinal changes in frequency of and bother from lower urinary tract symptoms in community dwelling men. J Urol 2002 Oct;168(4 Pt 1):1446-52.

216. Bosch JL. Urodynamic effects of various treatment modalities for benign prostatic hyperplasia. J Urol 1997 Dec;158(6):2034-44.

217. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992 Jun;30(6):473-83.

218. Batista-Miranda JE, Diez MD, Bertran PA, Villavicencio H. Quality-of-life assessment in patients with benign prostatic hyperplasia: effects of various interventions. Pharmacoeconomics 2001;19(11):1079-90.

219. Patrick DL, Deyo RA. Generic and disease-specific measures in assessing health status and quality of life. Med Care 1989 Mar;27(3 Suppl):S217-32.

220. McHorney CA. Generic health measurement: past accomplishments and a measurement paradigm for the 21st century. Ann Intern Med 1997 Oct 15;127(8 Pt 2):743-50.

221. Epstein RS, Deverka PA, Chute CG, Panser L, Oesterling JE, Lieber MM, Schwartz S, Patrick D. Validation of a new quality of life questionnaire for benign prostatic hyperplasia. J Clin Epidemiol 1992 Dec;45(12):1431-45.

222. Oh BR, Kim SJ, Moon JD, Kim HN, Kwon DD, Won YH, Ryu SB, Park YI. Association of benign prostatic hyperplasia with male pattern baldness. Urology 1998 May;51(5):744-8.

223. Lukacs B, Comet D, Grange JC, Thibault P. Construction and validation of a short-form benign prostatic hypertrophy health-related quality-of-life questionnaire. BPH Group in General Practice. Br J Urol 1997 Nov;80(5):722-30.

224. Welch G, Weinger K, Barry MJ. Quality-of-life impact of lower urinary tract symptom severity: results from the Health Professionals Follow-up Study. Urology 2002 Feb;59(2):245-50.

225. Salinas Sanchez AS, Hernandez Millan IR, Segura Martin M, Lorenzo Romero JG, Virseda Rodriguez JA. The impact of benign prostatic hyperplasia surgery on patients' quality of life. Urol Int 2002;68(1):32-7.

226. Arocho R, McMillan CA, Sutton-Wallace P. Construct validation of the USA-Spanish version of the SF-36 health survey in a Cuban-American population with benign prostatic hyperplasia. Qual Life Res 1998 Feb;7(2):121-6.

227. Brazier JE, Harper R, Jones NM, O'Cathain A, Thomas KJ, Usherwood T, Westlake L. Validating the SF-36 health survey questionnaire: new outcome measure for primary care. BMJ 1992 Jul 18;305(6846):160-4.

228. MacDonagh RP, Cliff AM, Speakman MJ, O'Boyle PJ, Ewings P, Gudex C. The use of generic measures of health-related quality of life in the assessment of outcome from transurethral resection of the prostate. Br J Urol 1997 Mar;79(3):401-8.

229. van Agt HM, Essink-Bot ML, Krabbe PF, Bonsel GJ. Test-retest reliability of health state valuations collected with the EuroQol questionnaire. Soc Sci Med 1994 Dec;39(11):1537-44.

230. Girman CJ, Jacobsen SJ, Rhodes T, Guess HA, Roberts RO, Lieber MM. Association of health-related quality of life and benign prostatic enlargement. Eur Urol 1999 Apr;35(4):277-84.

231. Revicki DA, Leidy NK, Howland L. Evaluating the psychometric characteristics of the Psychological General Well-Being Index with a new response scale. Qual Life Res 1996 Aug;5(4):419-25.

232. Doll HA, Black NA, Flood AB, McPherson K. Criterion validation of the Nottingham Health Profile: patient views of surgery for benign prostatic hypertrophy. Soc Sci Med 1993 Jul;37(1):115-22.

233. Krongrad A, Granville LJ, Burke MA, Golden RM, Lai S, Cho L, Niederberger CS. Predictors of general quality of life in patients with benign prostate hyperplasia or prostate cancer. J Urol 1997 Feb;157(2):534-8.

234. Morrow GR, Lindke J, Black P. Measurement of quality of life in patients: psychometric analyses of the Functional Living Index-Cancer (FLIC). Qual Life Res 1992 Oct;1(5):287-96.

235. Stewart AL, Ware JE, Sherbourne DC, Wells KB. Psychological distress/well-being and cognitive functioning measures. In: Stewart AL, Ware JE, editors. Measuring functioning and well-being: the medical outcomes study approach. Durham (NC): Duke University Press; 1992. p. 102-42.

236. Ramsey EW, Dahlstrand C. Durability of results obtained with transurethral microwave thermotherapy in the treatment of men with symptomatic benign prostatic hyperplasia. J Endourol 2000 Oct;14(8):671-5.

237. Puppo P. Long-term effects on bph of medical and instrumental therapies. Eur Urol 2001 Mar;39 Suppl 6:2-6.

238. Dull P, Reagan RW Jr, Bahnson RR. Managing benign prostatic hyperplasia. Am Fam Physician 2002 Jul 1;66(1):77-84.

239. Barry MJ, Mulley AG Jr, Fowler FJ, Wennberg JW. Watchful waiting vs immediate transurethral resection for symptomatic prostatism. The importance of patients' preferences. JAMA 1988 May 27;259(20):3010-7.

240. Bisonni RS, Lawler FH, Holtgrave DR. Transurethral prostatectomy versus transurethral dilatation of the prostatic urethra for benign prostatic hyperplasia: a cost-utility analysis. Fam Pract Res J 1993 Mar;13(1):25-36.

241. Blute M, Ackerman SJ, Rein AL, Beusterien K, Sullivan EM, Tanio CP, Strauss MJ, Manyak MJ. Cost effectiveness of microwave thermotherapy in patients with benign prostatic hyperplasia: part II--results. Urology 2000 Dec 20;56(6):981-7.

242. Manyak MJ, Ackerman SJ, Blute ML, Rein AL, Buesterien K, Sullivan EM, Tanio CP, Strauss MJ. Cost effectiveness of treatment for benign prostatic hyperplasia: an economic model for comparison of medical, minimally invasive, and surgical therapy. J Endourol 2002 Feb;16(1):51-6.

243. Bleichrodt H, Johannesson M. Standard gamble, time trade-off and rating scale: experimental results on the ranking properties of QALYs. J Health Econ 1997 Apr;16(2):155-75.

244. Cher DJ, Miyamoto J, Lenert LA. Incorporating risk attitude into Markov-process decision models: importance for individual decision making. Med Dec Making 1997 Jul-Sep;17(3):340-50.

245. Sox HC Jr, Blatt MA, Higgins MC, Marton KI. Medical decision making. Newton (MA): Butterworth-Heinemann; 1988. 406 p.

246. Lenert LA, Ziegler J, Lee T, Unfred C, Mahmoud R. The risks of multimedia methods: effects of actor's race and gender on preferences for health states. J Am Med Inform Assoc 2000 Mar-Apr;7(2):177-85.

247. Armstrong K, Schwartz JS, Fitzgerald G, Putt M, Ubel PA. Effect of framing as gain versus loss on understanding and hypothetical treatment choices: survival and mortality curves. Med Decis Making 2002 Jan-Feb;22(1):76-83.

248. Dolan P, Gudex C. Time preference, duration and health state valuations. Health Econ 1995 Jul-Aug;4(4):289-99.

249. Schelin S. Mediating transurethral microwave thermotherapy by intraprostatic and periprostatic injections of mepivacaine epinephrine: effects on treatment time, energy consumption, and patient comfort. J Endourol 2002 Mar;16(2):117-21.

250. Isotalo T, Talja M, Hellstrom P, Perttila I, Valimaa T, Tormala P, Tammela TL. A double-blind, randomized, placebo-controlled pilot study to investigate the effects of finasteride combined with a biodegradable self-reinforced poly L-lactic acid spiral stent in patients with urinary retention caused by bladder outlet [truncated]. BJU Int 2001 Jul;88(1):30-4.

251. Wada S, Yoshimura R, Kyo M, Hase T, Masuda C, Watanabe Y, Ikemoto S, Kawashima H, Kishimoto T. Comparative study of transurethral laser prostatectomy versus transurethral electroresection for benign prostatic hyperplasia. Int J Urol 2000 Oct;7(10):373-7.

252. Djavan B, Shariat S, Fakhari M, Ghawidel K, Seitz C, Partin AW, Roehrborn CG, Marberger M. Neoadjuvant and adjuvant alpha-blockade improves early results of high- energy transurethral microwave thermotherapy for lower urinary tract symptoms of benign prostatic hyperplasia: a randomized, prospective clinical trial. Urology 1999 Feb;53(2):251-9.

253. Lukkarinen O, Lehtonen T, Talja M, Lundstedt S, Tiitinen J, Taari K. Finasteride following balloon dilatation of the prostate. A double-blind, placebo-controlled, multicenter study. Ann Chir Gynaecol 1999;88(4):299-303.

254. Shalev M, Richter S, Kessler O, Shpitz B, Fredman B, Nissenkorn I. Long-term incidence of acute myocardial infarction after open and transurethral resection of the prostate for benign prostatic hyperplasia. J Urol 1999 Feb;161(2):491-3.

255. Eliasson T, Terio H, Damber JE. Transurethral microwave thermotherapy for benign prostatic hyperplasia--experience with the Prostcare. World J Urol 1998;16(2):109-14.

256. Devonec M, Dahlstrand C. Temporary urethral stenting after high-energy transurethral microwave thermotherapy of the prostate. World J Urol 1998;16(2):120-3.

257. Horninger W, Janetschek G, Watson G, Reissigl A, Strasser H, Bartsch G. Are contact laser, interstitial laser, and transurethral ultrasound-guided laser-induced prostatectomy superior to transurethral prostatectomy. Prostate 1997 Jun 1;31(4):255-63.

258. Abbou CC, Colombel M, Payan C, Beurton D, Viens-Bitker C, Richard F, Gibod LB, Leduc A, Jardin A, Chatelain C, et al.. The efficacy of microwave induced hyperthermia in the treatment of BPH: the Paris public hospitals' experience. Prog Clin Biol Res 1994;386:449-53.

259. de Wildt MJ, Hubregtse M, Ogden C, Carter SS, Debruyne FM, De la Rosette JJ. A 12-month study of the placebo effect in transurethral microwave thermotherapy. Br J Urol 1996 Feb;77(2):221-7.

260. te Slaa E, De Wildt MJ, Debruyne FM, De Graaf R, De La Rosette JJ. Urinary tract infections following laser prostatectomy: is there a need for antibiotic prophylaxis? Br J Urol 1996 Feb;77(2):228-32.

261. Anderson TF, Bronnum-Hasen H, Sejr T, Roepstorff C. Elevated mortality following transurethral resection of the prostate for benign prostatic hypertrophy. But why? Med Care 1990;28:870-9.

262. Roos NP, Wennberg JE, Malenka DJ, Fisher ES, McPherson K, Andersen TF, Cohen MM, Ramsey E. Mortality and reoperation after open and transurethral resection of the prostate for benign prostatic hyperplasia. N Engl J Med 1989 Apr 27;320(17):1120-4.

263. Edwards L, Powell C. An objective comparison of transurethral resection and bladder neck incision in the treatment of prostatic hypertrophy. J Urol 1982 Aug;128(2):325-7.

264. Cranovsky R, Matillon Y, Banta D. EUR-ASSESS project subgroup report on coverage. Int J Technol Assess Health Care 1997 Spring;13(2):287-332.

265. Krumins PE, Fihn SD, Kent DL. Symptom severity and patients' values in the decision to perform a transurethral resection of the prostate. Med Decis Making 1988 Jan-Mar;8(1):1-8.

266. Llewellyn-Thomas HA, Williams JI, Levy L, Naylor CD. Using a trade-off technique to assess patients' treatment preferences for benign prostatic hyperplasia. Med Decis Making 1996 Jul-Sep;16(3):262-82.

Appendix A: Description of Outcome Measures

Trials of treatments for benign prostatic hyperplasia (BPH) examine the effects of treatment on several outcomes. These outcomes may be either beneficial or harmful. Below, we first discuss outcomes that measure potential benefits, and subsequently we describe several potential harms.

Potential Benefits

There are three categories of benefits of treatments for BPH: symptoms, physiological measures, and quality of life. *Symptoms* and *quality of life* (QoL) are subjective, patient-oriented measures obtained using questionnaires completed by patients, whereas physiological measures are objective measures determined by physicians using systematic instrumented measurements of the functioning of the lower urinary tract. These categories are further defined and described below.

The literature on BPH distinguishes between measurements of a patient's *symptoms,* and the degree to which the patient is *bothered* by those symptoms. This is because two patients can have the same level of symptoms, and one patient may be greatly bothered while the other is relatively unbothered. We discuss degree of bother in the section on quality of life.

Symptoms

Men with BPH experience many symptoms due to enlargement of the prostate. These include a high frequency of urination, pushing or straining during urination, or a painful or burning sensation during urination. To measure symptom severity, clinical trials often use a questionnaire that is completed by the patient. Using a *standardized* questionnaire ensures that different patients are asked precisely the same questions about their symptoms. Further, if different trials use the same questionnaire, then one can compare the degree of symptom improvement across trials. The most commonly used questionnaire is the International Prostate Symptom Score (IPSS)[5], which appears in Table A- 1.(20) It contains seven questions related to prostate symptoms, and the scores for each question are added to yield a single summary score. The summary score ranges from zero (indicating no symptoms) to 35 (indicating very severe symptoms). A score of seven or less indicates mild symptoms, a score between eight and 19 indicates moderate symptoms, and a score of 20 or higher indicates severe symptoms.(20) Although these cutoff points are arbitrary, a recent review article suggested that this categorization can be used to identify patients with mild symptoms who generally do not require treatment, or to identify patients with severe symptoms for whom treatment is more urgent.(197) The IPSS requires only a sixth-grade reading level,(198) it has been translated into many languages,(197) and it has been recommended for use by the International Consultation

[5] The IPSS is also known as the American Urologist Association Symptom Score (AUA).

on BPH.(199) An estimated 99% of urologists are aware of the IPSS, and 63% use it in clinical practice.(199)

In addition to the IPSS, several other BPH symptom questionnaires have been developed (Table A- 2). All of these questionnaires contain questions similar to those in the IPSS (e.g., nighttime frequency of urination, weak urinary flow, incomplete emptying of the bladder). Some pose questions not in the IPSS, such as questions about hesitancy before urination and post-urinary dribbling. All of the questionnaires employ slightly different wording and use different response scales that could potentially influence patients' scores. However, the correlations between questionnaires are all high (published correlations range from 0.51 to 0.93),(200,201) indicating that they measure similar aspects of patients' BPH symptoms.(200)

All of the symptom questionnaires rely on patients' memories of their recent symptoms. Because memories are imperfect, it is important to assess both the *validity* and *reliability* of symptom questionnaires. Validity refers to whether a questionnaire measures what it is intended to measure. In the present context, there is no "gold standard" for the patient's true symptoms, so one cannot assess validity in the strictest sense. Consequently, researchers have attempted to assess validity indirectly (specifically, "construct" validity) by determining whether patients' scores on a symptom questionnaire correlate well with other relevant measures, such as whether patients report global improvement after treatment. If they do, then the questionnaire is said to have construct validity. This has been established for three of the questionnaires listed in Table A- 2. The IPSS correlates well with the degree to which patients were bothered by their symptoms,(20) patient global ratings of improvement after treatment,(202) and global ratings of bother.(20) The Dan-PSS(203) and the ICSmaleSF(204) also correlate well with these measures.

Reliability refers to the repeatability of a questionnaire. Two types of reliability are usually investigated: *test/retest reliability* and *internal consistency*. Test-retest reliability concerns whether the same patient gives the same answers at different times. For example, a patient could complete a symptom questionnaire on March 1st, and then complete it again on April 1st. If the patient gives the same responses, then the test has good test-retest reliability (assuming there was no treatment intervention during the month of March). Internal consistency addresses whether responses to individual questions in the questionnaire are correlated, and if so, they are believed to measure the same underlying construct. Empirical trials have found good test-retest reliability (Pearson r 0.8-0.9) and good internal consistency reliability (Cronbach's alpha 0.7-0.8) for three symptom questionnaires (the same three for which validity has been established): the IPSS,(20) the Dan-PSS,(203) and the ICSmaleSF.(204)

Despite the fact that these questionnaires are reliable and valid, there are challenges to using them to measure the effect of treatment. This is because patients generally expect to improve after treatment. Thus, they may report fewer symptoms after treatment even if there was no real improvement.(24) This possibility is strong motivation for the use of a blinded control group in any trial of BPH treatment. Patients in both groups (the treatment group and the control group) might expect to improve, thus any comparison between groups must factor out any effect of patients' expectations.

Ideally, patients in the control group would receive a placebo, because the placebo effect is a well-established finding in BPH research. In a review of 1,417 patients in 45 placebo arms of BPH clinical trials, Roehrborn (1996)(205) found that 42% of placebo-treated patients experienced an improvement in their symptoms after "treatment." In addition, the review noted that the Food and Drug Administration and the World Health Organization "advocate rather strictly the use of placebo controls" (p 242) in the field of BPH research.(205)

Expectation is less likely to affect more objective outcome measures, such as the physiological measures described in the next section. However, as discussed below, these physiological measures are an indirect way to measure the most important outcomes of treatments for BPH.

Table A- 1. International Prostate Symptom Score (IPSS)

Question	Not at All	Less Than 1 Time in 5	Less Than Half the Time	About Half the Time	More Than Half the Time	Almost Always
Over the past month, how often have you had a sensation of not emptying your bladder completely after you finish urinating?	0	1	2	3	4	5
Over the past month, how often have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5
Over the past month, how often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5
Over the last month, how difficult have you found it to postpone urination?	0	1	2	3	4	5
Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5
Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5
Quality of life question (IPSS QOL)						
	None	**1 Time**	**2 Times**	**3 Times**	**4 Times**	**5 + Times**
Over the past month, how many times did you most typically get up to urinate from the time you went to bed until the time you got up in the morning?	0	1	2	3	4	5

The scores for each question are added to yield the summary symptom score, which ranges from 0 (indicating no symptoms) to 35 (indicating very severe symptoms).(20)

Table A- 2. Symptom Questionnaires

Questionnaire	Primary reference	Number of questions	Validity?	Reliability?
Boyarsky[a]	Boyarsky et al. (1977)(206)	9		
Madsen and Iversen	Madsen and Iversen (1983)(21)	9		
IPSS (AUA)[b]	Barry et al. (1992)(20)	7	✓	✓
Dan-PSS	Hansen et al. (1995)(203)	12	✓	✓
ICSmaleSF	Donovan et al. (2000)(207)	11	✓	✓

IPSS - International Prostate Symptom Score (also called the American Urologist Association Symptom Score)
Dan-PSS - Danish Prostatic Symptom Score
ICSmaleSF - International Continence Society Symptom Frequency for males

a Bolognese(208) proposed a slight alteration of the Boyarsky scale, thus it is not listed in the table.
b The Maine Medical Assessment Program questionnaire(209) was an early version of the IPSS, thus it is not listed in the table

✓ - Indicates that reliability or validity have been tested and confirmed (see explanation in text)

Physiological measures

BPH involves an enlargement of the prostate that decreases bladder capacity and restricts the flow of urine. Thus, physiological measures such as prostate size, speed of urine flow, and pressure on the urethra are reported in trials of treatments for BPH. The commonly reported physiological measures are listed and described in Table A-3.

Physiological measures are relevant because they are objective measures of physiological causes of the symptoms of BPH. If these measures really do reflect the causes of the symptoms, then one would expect high correlations between physiological measures and symptom scores. Several trials have investigated such correlations, and all have concluded that they are low.(210-213) For example, a 1995 trial by Bosch, Hop, Kirkels et al.(212) found only a small correlation (Spearman r = 0.19) between symptom scores on the IPSS and prostate volume (a list of the published correlations appears in Table A-4). This suggests that, on average, there is a slight tendency for men with more symptoms to have larger prostates. However, it also suggests that there were some men with mild symptoms and large prostates, and there were other men with severe symptoms but small prostates. Consequently, prostate size itself does not adequately explain why some men have mild symptoms and others have severe symptoms.

Given the absence of strong correlations between symptoms and physiological measures, which outcome category is more important in assessing the efficacy of treatments for BPH? Symptom scores are more patient-oriented: a patient cares more about his symptoms than the actual speed of urinary flow or the size of his prostate. The physiological measures, therefore, are indirect measures of what matters to patients.

Thus, in the face of a discrepancy between symptom scores and physiological measures, a patient-oriented analysis would emphasize the symptom scores. However, symptom scores are vulnerable to expectation effects, whereas physiological measures are relatively free from such effects. Expectation effects on symptom scores motivate the need for blinded control groups in BPH treatment trials, because the expectation effects would be cancelled out in any between-groups comparison.

Although physiological measures are less susceptible to placebo effects than are symptom scores, they are still susceptible to a statistical artifact called *regression to the mean*.(24) Symptoms of BPH fluctuate over time,(214,215) and patients tend to be recruited into trials when they are relatively sick (i.e., when they meet stringent inclusion criteria).(24) An observed "improvement", therefore, may simply reflect a return to the patient's typical level of health.[6] For example, a patient could be recruited into a trial when he had a relatively slow urinary flow rate (a physiological measure). During the trial, the patient's flow rate could be faster, not because of the treatment, but instead because the trial observed a more typical flow rate for that patient (i.e., closer to that patient's mean). Regression to the mean provides further motivation for the use of a control group in any clinical trial of BPH. Patients in different groups but the same selection criteria would likely experience the same amount of regression to the mean, so the between-groups comparison would not be confounded.

[6] The "improvement" could also be due to a placebo effect. Both of these possibilities (regression-to-the-mean and a placebo effect) are contrary to the claim that the improvement was actually caused by the treatment. For a detailed discussion of this point, see Sech, Montoya, Bernier et al. (1998).(24)

Table A- 3. Physiological measures

Measure (abbreviation)	Description
Peak urinary flow rate (Q_{max})	During urination, the maximum amount of urine expelled per minute (measured in liters per minute or milliliters per minute). Higher values indicate better outcomes.
Voided volume	The amount of urine expelled during urination (measured in liters or milliliters). Higher values indicate better outcomes.
Postvoid Residual Volume (PVR)	After urination, the amount of urine remaining in the bladder (measured in liters or milliliters). Lower values indicate better outcomes.
Relative Residual Volume	The percentage of urine remaining in the bladder after urination. Lower values indicate better outcomes.
Prostate volume	Size of the prostate (measured in cubic centimeters). Lower values indicate better outcomes.
Detrusor pressure at peak urinary flow	During urination, the amount of pressure on the urethra (measured in number of centimeters water) at the time of peak urinary flow. Lower values indicate better outcomes.
Urethral resistance factor	During urination, the amount of pressure on the urethra (measured in number of centimeters water) at zero flow rate, interpolated from a plot of flow rate and pressure. See Bosch(216) for details. Lower values indicate better outcomes.
Minimal urethral opening pressure	During urination, the minimum amount of pressure on the urethra (measured in number of centimeters water) at the beginning of urination, interpolated from a plot of flow rate and pressure. See Bosch(216) for details. Lower values indicate better outcomes.
Prostate specific antigen (PSA)	An antigen in the blood that is released by the prostate (measured in nanograms per milliliter). Lower levels of this antigen indicate better outcomes.

Table A- 4. Correlations between physiological measures and symptom scores

Physiological measure	Correlation with symptom scores[a]
Maximum flow rate (Q_{max})[b]	-0.07(210) -0.12(211) -0.18(212) -0.24(213)
Average flow rate	-0.13(210) -0.25(213)
Postvoid residual volume (PVR)	0.01(210) 0.05(211) 0.25(212)
Relative residual volume	0.10(211)
Voided volume	-0.21(213)
Total prostate volume[c]	-0.09(210) 0.03(211) 0.19(212)
Central prostate volume[d]	0.24(212)
Prostate specific antigen (PSA)	-0.06(210)
Obstruction grade[e]	0.02(211)

[a] Symptom score as measured by the International Prostate Symptom Score (IPSS)
[b] Donovan, Abrams, Peters et al. (1996](204) also found a weak relation between maximum flow rate and symptom scores, but they did not report the value of the correlation.
[c] Simpson, Fisher, Lee et al. (1996](213) computed the correlation between total prostate volume and symptom scores, and found "no statistically significant relation", but they did not report the value of the correlation.
[d] Volume of the central part of the prostate.
[e] Obstruction grade is an urodynamic parameter derived from the minimal urethral opening pressure.(211)

Quality of life

Some trials report how treatments of BPH affect patients' overall quality of life (QOL). This is a more general outcome measure than symptoms, physiological measures, or adverse events, because QOL can incorporate cognitive abilities, activities of daily living, and family relationships. With regard to BPH, QOL measures can assess the *bothersomeness* of a patient's symptoms. Two patients can have identical symptoms, but one patient may be greatly bothered by those symptoms and the other patient relatively unbothered.

Quality of life questionnaires can be grouped into two categories: *disease-specific* and *generic*. Disease-specific questionnaires only contain questions about how BPH itself affects quality of life. For example, one disease-specific question is: "If you were to spend the rest of your life with your prostate symptoms just as they are now, how would you feel about that?"(20) Patients respond on a 0-6 scale where 0 means "delighted" and 6 means "terrible." By contrast, a generic QOL questionnaire does not refer to any particular disease, but instead contains questions about the patients' QOL in general.

For example, one question in the Short Form 36 (SF-36) asks: "During the past 4 weeks, how much did pain interfere with your normal work (including work both outside the home and housework)?"(217) Patients respond on a 0-4 scale where 0 means "not at all" and 4 means "extremely." Disease-specific questionnaires are more sensitive than generic questionnaires to BPH treatment effects.(218-220)

A list of the QOL questionnaires that have been used to assess BPH treatments appears in Table A- 5. Some questionnaires consist of only one question,(20,207) whereas one contains 44 questions.(221) As with the symptom questionnaires discussed earlier, all of these questionnaires are vulnerable to expectation effects, and the use of blinded control groups can address this difficulty.

Table A- 5. Quality of life questionnaires

	Number of questions	Description
Disease-specific quality of life questionnaires		
BPH Impact Index	4	Questions about the bothersomeness of specific BPH symptoms, including physical discomfort, worry, trouble with urination, and prevention of normal activities. Summary score ranges from 0 to 13 where 0 indicates no bother and 13 indicates extreme bother.(202)
Global question[a]	1	"If you were to spend the rest of your life with your prostate symptoms just as they are now, how would you feel about that?" (0 = Delighted, 1 = Pleased, 2 = Mostly satisfied, 3 = Mixed, 4 = Mostly dissatisfied, 5 = Unhappy, 6 = Terrible)(20)
Bothersomeness questions in Dan-PSS	12	Questions about the bothersomeness of specific BPH symptoms. Each question corresponds to a symptom question in the Dan-PSS.(203) The summary score for bother ranges from 0 to 36 where 0 indicates no bother and 36 indicates extreme bother.
ICSQoL single question[b]	1	"Overall, how much do your urinary symptoms interfere with your life?" (0 = not at all, 1 = a little, 2 = somewhat, 3 = a lot)(207)
ICSQoL	6	Questions about bothersomeness of symptoms and interference with daily life.(222)
QOL9	9	Ratings from 0-10 for each of nine domains. Minimum score is 0, maximum score is 90.(223)
Epstein	44	Questions in each of six domains. Minimum score is 0, maximum score is 239.(221)
Generic quality of life questionnaires		
Short Form-36 (SF-36)	36	Questions in each of eight domains: physical functioning, role limitations due to physical problems, social functioning, bodily pain, general mental health, role limitations due to emotional problems, vitality, and general health perceptions.(217,224-227)
EuroQOL	14	Questions in each of six domains: mobility, self-care, usual activities, pain/discomfort, mood, and general health.(228,229)
Psychological General Well Being	22	Questions in each of five domains: depression, anxiety, self-control, vitality, and positive attitude.(230,231)
Nottingham Health Profile	38	Questions in each of six domains: energy level, pain, emotional reaction, sleep, physical mobility, and social isolation.(228,232)

Functional Living Index - Cancer	22	Questions related to social support, activities of daily living and other domains.(233,234)
Rand Mental Health Index-17	17	Questions in five domains of psychological distress and well-being: anxiety, depression, behavioral-emotional control, belonging/loneliness, and positive affect.(233,235)

[a] This is an optional add-on to the International Prostate Symptom Score (IPSS).
[b] This is an optional add-on to the International Continence Society Symptom Frequency for males (ICSmaleSF).

SF-36 Short Form 36
Dan-PSS Danish Prostatic Symptom Score
EuroQOL-5D European quality of life questionnaire, version 5D

Potential Harms

Treatments can have harms as well as benefits. In this section, we discuss three categories of potential harms that can be caused by treatments for BPH: perioperative outcomes, adverse events and retreatment. *Perioperative* outcomes occur during the operation (or soon after), *adverse events* can occur soon after the operation or after a delay, and *retreatment* involves the long-term question of whether a treatment ultimately results in the need for additional treatment (due to the lack of benefit or declining benefit). These outcomes are further addressed in the Results sections of this report.

Perioperative outcomes

Patients receiving certain surgical treatments can require transfusions. Thus, trials often report the number of patients who required transfusions, the amount of blood loss, and the amount of blood that was transfused. Additional intraoperative measures included operation time, anesthesia usage, and the amount of prostate tissue resected. Immediately after the operation, most treatments for BPH require urethral catheterization, so many trials report the number of days that patients were catheterized as well as the length of hospitalization. Some trials also report postoperative changes in serum levels of hemoglobin, hematocrit, sodium, or other variables that are affected by the mixing of irrigation fluids with the patients' blood during the operation.

Adverse events

All treatments for BPH are associated with some adverse events. For any treatment decision, one should consider both the frequency and the severity of adverse events. These are weighed against the potential benefits of a treatment. The choice between treatments involves a tradeoff between efficacy and adverse events, in which a treatment with greater efficacy, but more potential adverse events, is compared to an alternative treatment with lower efficacy, but fewer adverse events.

Some events are experienced soon after treatment, whereas others are experienced after a few weeks or months. The commonly reported adverse events of treatments for BPH are listed and described in Table A- 6. Additional potential adverse events include mortality, myocardial infarction, stroke, deep venous thrombosis, fever, impaired ejaculation, and decreased libido. Surgical techniques (such as transurethral resection of the prostate, or TURP) are associated with different categories of adverse events than non-surgical techniques (such as transurethral microwave thermotherapy, or TUMT). For example,

some patients experience blood loss requiring transfusion after TURP, but none experience it after TUMT.(6)

Table A- 6. Adverse events

Adverse event	Description
Bladder neck contracture	Shortening of muscle tissue in the bladder neck
Dilutional hyponatremia	Inadequate sodium in the blood
Dysuria	Pain (burning sensation) or difficulty in urination
Impotence	Inability to achieve or maintain an erection
Retrograde ejaculation	Ejaculation in which semen travels backwards towards the bladder
Urinary retention	Inability to initiate urination
Urethral stricture (stenosis)	Narrowing or closing of the urethra
Urinary incontinence	Inability to control the flow of urine, resulting in dribbling.
Urinary tract infection (UTI)	Infection of the urinary tract

Retreatment

For some patients with BPH, the original treatment does not relieve symptoms or the relief is temporary, and it is necessary to retreat the patient. This provides evidence against the efficacy of the original treatment. If the original treatment had worked, then retreatment would not be necessary. The retreatment can be a repetition of the original treatment, or it can be a different treatment altogether. If one wishes to compare any two treatments, an important consideration is which treatment is associated with a lower (i.e., better) rate of retreatment. A related issue is which treatment is associated with a greater amount of time before retreatment.

Several reviews have argued that retreatment is a useful outcome measure in treatments for BPH.(6,236-238) It is an objective measure of a patient-oriented outcome. Patients care about the need for retreatment because they must endure the persistence of symptoms as well as any adverse events caused by the retreatment.

Despite compelling reasons for measuring retreatment, many trials do not report it. One possible reason for this is the need for sufficient followup time. If a trial has a short followup period, then it is less able to detect patients who require retreatment.

Even if a trial has long-term followup, there may still be difficulties with comparing retreatment rates between treatments. One difficulty concerns patient selection bias. If the patients who received one treatment were systematically different from patients who received the other treatment (e.g., they had more severe symptoms before treatment), then a simple comparison of retreatment rates would be biased. This difficulty can be addressed by randomly assigning patients to treatments. Another difficulty is that treatment failure does not necessarily imply the need for retreatment. Some patients may experience the failure of a treatment, but their symptoms are not severe enough to justify retreatment.

Appendix B: Description of Utilities

This section focuses on patients' reactions to the outcomes of BPH treatments (or more specifically, "utilities", described in detail below). We first provide background information on what utilities are and how they are measured. Then, we review the evidence on patients' utilities for the outcomes of treatments for BPH.

Background on utilities

The word "utility" in medical decision making refers to the relative amount of value or worth that a patient places on a given outcome.[7] Utility is measured on a scale from 0 to 1 where 0 indicates the lowest possible utility and 1 indicates the highest possible utility. Suppose a patient is asked how he would feel if he had severe incontinence. If a patient places a relatively low utility (such as 0.25) on this health state, then this means that he perceives it quite negatively. Alternatively, if the patient assigns a relatively high utility to this health state (e.g., 0.85), then he does not think it would be so bad. Using utilities, a patient can express his opinions about the relative values of different outcomes. The concept of utility has been used in a medical decision analysis of BPH treatments to compare the overall desirability of different treatments.(239) Also, utilities have been employed in cost-effectiveness analyses[8] of BPH treatments.(22,240-242)

Utilities can be measured in several ways. Here, we describe two methods for measuring utilities: the time tradeoff (TTO) and the standard gamble (SG). The time tradeoff method (TTO) presents patients with a series of hypothetical choices. By asking the patient to state his preferences between hypothetical alternatives, the researcher can determine the degree of subjective value or worth that the patient places on an outcome. The central issue is how many years of life the patient is willing to give up in order to avoid living with a debilitating health state. If a patient perceives the health state as being extremely poor, then he may be willing to live a shorter life if it means he could avoid the debilitating health state. For example, to determine a patient's TTO utility for severe incontinence, a researcher would first ask the patient to choose between the following two hypothetical alternatives:

Alternative A: You live for the next 10 years with severe incontinence, after which you would die painlessly.

Alternative B: You live for the next 9 years in perfect health (i.e., no symptoms of BPH), after which you would die painlessly.

[7] The concept of utility was introduced by economists to explain why different people perceive the value of money differently. Researchers have applied utilities to medical decision analysis by computing an "expected utility" for each treatment, and the treatment with the highest expected utility is preferred. An introduction to this topic appears in a book by Sox, Blatt, Higgins, et al. (1988).(245) Utilities are also used as quality weights in quality-adjusted life years ("QALYs") as a way to compare treatments for their combined effects on quality and quantity of life.(264)

[8] A cost-effectiveness analysis that uses utilities to measure effectiveness is also referred to as a "cost-utility" analysis.

Some patients may be willing to give up a year of life in order avoid severe incontinence, but other patients may not be willing. If the patient prefers Alternative A, then the researcher presents another hypothetical choice in which Alternative B is made more attractive by increasing the number of years in perfect health (e.g., to 9.5 years).[9] The patient is then asked to choose between these new Alternatives A and B. The process continues until the patient is *indifferent* between the two alternatives (i.e., A and B are equally preferable). The point of indifference determines the patient's utility. For example, suppose the patient is indifferent between Alternatives A and B when Alternative B is 8.5 years in perfect health. This would mean that the patient's TTO utility for severe incontinence is 8.5/10 or 0.85.

Like the TTO, the standard gamble method (SG) requires patients to make choices between hypothetical alternatives. Unlike the TTO, however, the SG uses the concept of risk. For example, suppose one wants to determine a patient's SG utility for severe incontinence. To measure this utility, Ackerman, Rein, Blute, et al. (2000)(22) asked patients with BPH to choose between the following hypothetical alternatives:

Alternative A: Severe incontinence. You have undergone treatment for BPH that results in a total loss of voluntary control over urination.

Alternative B: A gamble in which there is a 90% chance of having perfect health (i.e., no BPH symptoms and no adverse events), but there is a 10% chance of death.

If the patient prefers Alternative A, then Alternative B is made more attractive by increasing the chance of perfect health (e.g., to 95%) and decreasing the chance of death (e.g., to 5%),[10] and the patient is asked to choose between these new Alternatives A and B. As with the TTO, the process continues until the patient is indifferent between the two alternatives. The point of indifference determines the patient's utility. For example, suppose the patient is indifferent between Alternatives A and B when Alternative B is a 95% chance of perfect health and a 5% chance of death. This would mean that the patient's utility for severe incontinence is 95/100 or 0.95.

The two methods approach the problem differently, and they can produce different results.(243) The SG (but not the TTO) incorporates patient's attitudes towards risk, and because patients tend to be averse to risks,(244) the SG is assumed to be as the "gold standard" for utility measurement.(245)

One difficulty with utility measurement concerns the hypothetical nature of the elicitation process. Both methods require the patient to *imagine* what it would be like to live in a specific health state. The patient's responses are based, therefore, on his imagined response to this health state, which may be different from his true response to the health state if he actually experienced it. However, this difficulty is not unique to utility

[9] If the patient prefers Alternative B, then Alternative B is made less attractive by decreasing the number of years in perfect health (e.g., to 8.5 years). The process continues until the patient is indifferent between the alternatives.

[10] If the patient prefers Alternative B, then Alternative B is made less attractive by decreasing the chance of perfect health (e.g., to 85%) and increasing the chance of death (e.g., to 15%). The process continues until the patient is indifferent between the alternatives.

measurement. In any medical treatment, outcomes may occur that the patient has never experienced, and the patient's reaction to those outcomes cannot be known in advance.

A more fundamental difficulty with utility measurement concerns the quantifiability of patient's values. Both methods attempt to assign a number to a patient's opinion about a health state. This number may depend on many unintended factors, such as the way the health state is described(246) or the manner in which the choice is framed.(247) Also, a patient's opinion can change over time, suggesting that no single number can fully capture his beliefs about a health state.(248) With these caveats in mind, the next section reviews the available evidence on patients' utilities for the outcomes of BPH treatments.

Evidence on utilities for BPH

Only two studies have reported BPH patients' utilities (in their technical sense) for treatment outcomes.[11] Ackerman et al. (2000)(22) used the standard gamble to measure the preferences of 13 men with moderate to severe symptoms of BPH.[12] They reported the mean SG utilities for five short-term events and 17 long-term outcomes of BPH treatments. According to the mean SG utilities, patients perceive myocardial infarction as the worst among the five short-term events, followed by deep venous thrombosis. Among the long-term outcomes, patients perceived severe incontinence as the worst, followed by urinary retention. These utilities, which were 0.80 and 0.82, respectively, show that patients perceive these outcomes rather negatively. Also, note that there were three categories of remission: no remission, moderate remission, and significant remission. Within each of these categories, there was a consistent ordering of three adverse events: erectile dysfunction, urinary incontinence, and ejaculatory dysfunction. Specifically, the typical patient thought erectile dysfunction was worse than urinary incontinence, which was perceived to be worse than ejaculatory dysfunction.

Schulz et al. (2002)(23) used the time tradeoff (TTO) technique to measure utilities. They enrolled 29 patients with a mean I-PSS symptom score of 16.2, indicating that the typical patient had moderate LUTS. Each patient performed the time tradeoff task for each of two health states (current level of symptoms, and the worst possible level of symptoms) at each of two time intervals (1 year and 10 years). The mean TTO utilities (and ranges) appear in Table B- 2. The typical patient was willing to give up 14%-20% of time in order to relieve their current symptoms. When presented with a hypothetical situation involving the worst possible BPH symptoms,[13] the typical patient was willing to give up 46%-52% of time in order to avoid that scenario.

In summary, one study used the standard gamble method, whereas the other used the time tradeoff method. The study by Ackerman et al. (2000)(22) showed that the typical patient

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[11] Two additional studies addressed similar issues, but they are not discussed here for the following reasons. Krumins, Fihn and Kent (1988)(265) employed the time tradeoff (TTO) technique to measure the utilities of men with BPH, but they did not report summary statistics on the measured TTO utilities. Llewellyn-Thomas et al. (1996)(266) reported SG utilities of a group of men who were seen at a urology clinic for an initial diagnostic assessment for BPH, and some of them may not have had BPH.

[12] As measured by I-PSS symptom scores between 15 and 29, inclusive.

[13] As defined by an I-PSS score of 35, which is the maximum on this instrument.

was willing to risk death in order to avoid potential short term adverse events (such as myocardial infarction) and long-term outcomes (such as severe incontinence). The study by Schulz et al. (2002](23) found that the typical patient was willing to give up some of their lifespan in order to cure their current symptoms of BPH. Jointly, the studies indicate a clear desire on the part of patients both to cure their symptoms and to avoid adverse events. However, because there were only two studies, the findings prevent firm conclusions about patients' precise values.

Table B- 1. Mean standard gamble utilities in Ackerman et al. (2000)

Short-term events	Mean SG utility[1]	Range
Myocardial infarction	0.78	0.69 - 0.95
Deep venous thrombosis	0.89	0.74 - 0.99
Severe urinary tract infection	0.93	0.77 - 0.99
Urethral stricture/bladder neck contracture	0.94	0.78 - 1
Dysuria	0.97	0.83 - 1
Long-term outcomes[2]	**Mean SG utility**	**Range**
Severe incontinence	0.8	0.5 - 0.98
Urinary retention	0.82	0.5 - 1
Worsening BPH and ejaculatory dysfunction	0.9	0.78 - 1
Worsening BPH and no adverse events	0.92	0.78 - 1
No remission and erectile dysfunction	0.9	0.78 - 1
No remission and urinary incontinence	0.93	0.82 - 1
No remission and ejaculatory dysfunction	0.95	0.78 - 1
No remission and no adverse events	0.96	0.83 - 1
Moderate remission and erectile dysfunction	0.92	0.83 - 1
Moderate remission and urinary incontinence	0.94	0.82 - 1
Moderate remission and ejaculatory dysfunction	0.96	0.84 - 1
Moderate remission and no adverse events	0.98	0.92 - 1
Significant remission and erectile dysfunction	0.93	0.83 - 1
Significant remission and urinary incontinence	0.95	0.84 - 1
Significant remission and ejaculatory dysfunction	0.97	0.84 - 1
Significant remission and no adverse events	1	0.94 - 1

[1] These means were calculated by ECRI based on the means provided in Table I on page 975 of Ackerman, Rein, Blute, et al. (2000).(22) Values were rounded to the nearest 0.01.

[2] An additional long-term outcome was "moderate-to-severe BPH," which was identical to the outcome "No remission and no adverse events", thus it is not listed separately in the table. This outcome corresponds to *no* effect of the treatment (i.e., no benefit and no harm). The authors also reported utilities for three treatments for BPH, but these are not listed in the table because this section addresses the utilities for potential *outcomes* of treatments, not utilities for the treatments *per se*.

SG - Standard gamble utility (see explanation in text).

Table B- 2. Mean time tradeoff utilities in Schulz et al. (2002)

Health state	Time interval[1]	Mean TTO utility	Range
Current level of symptoms	1	0.86	0.13-1
Current level of symptoms	10	0.80	0.05-1
Worst possible level of symptoms[2]	1	0.54	0.04-1
Worst possible level of symptoms[2]	10	0.48	0.05-1

[1] The time interval refers to the time that the patient would spend in the corresponding health state. For example, in the first row, the typical patient was indifferent between living for 1 year with current symptoms and living for 0.86 years in perfect health. The second row indicates that the typical patient was indifferent between living for 10 years with current symptoms and living for 8 years (0.80 x 10) in perfect health.

[2] The worst possible level of symptoms was defined as an I-PSS score of 35, which is the highest (worst) possible score on that instrument.

TTO Time tradeoff (see explanation in text).

Appendix C: Literature Search Strategies

Electronic Database Searches

We searched the following databases for relevant information:

Cochrane Database of Systematic Reviews (through 2003, Issue 2)

Cochrane Registry of Clinical Trials (through 2003, Issue 2)

Cochrane Review Methodology Database (through 2003, Issue 2)

Database of Reviews of Effectiveness (Cochrane Library) (through 2003, Issue 2)

ECRI Health Technology Trends (through December 2002)

ECRI International Health Technology Assessment (IHTA) (1991 through January 2003)

ECRI Library Catalog (through January 2003)

ECRI TARGET (through January 2003)

Embase (Excerpta Medica) (1991 through December 26, 2002)

PsycINFO (1989 through December 26, 2002)

PubMed (MEDLINE, PreMEDLINE, HealthSTAR) (1975 through November 14, 2003)

TRIP Database (through December 5, 2002)

U.K. National Health Service Economic Evaluation Database (NHS EED) (through January 2003)

U.K. National Institute for Clinical Excellence (NICE) (through December 17, 2002)

U.S. National Guideline Clearinghouse™ (NGC™) (through January 2003)

PubMed searches

For PubMed, the following strategy was used to limit results to controlled clinical trials:

Controlled clinical trials:
(randomized controlled trials(164) OR random allocation(164) OR randomized controlled trial(8) OR double-blind method(164) OR single-blind method(164) OR "single-dummy" OR "double-dummy" OR controlled clinical trials(164) OR controlled clinical trial(8) OR placebo* OR controls[ab] OR "latin square"[tw])

All searches were limited to English language publications and human population. The following strategy was used for these limits:

English[la] AND (human(164) OR premedline(222) OR publisher(222))

Benign Prostatic Hyperplasia (BPH):

1) prostatic hyperplasia(164)
2) "bph" OR "benign prostatic hyperplasia"
3) (benign OR enlarg* OR hyperplasia OR hypertroph*) AND prostat*
4) "bladder outlet obstruction" AND (male(164) OR prostate OR prostatic)
5) #1 OR #2 OR #3 OR #4
6) #5 NOT (adenoma* OR adenocarcinoma* OR neoplasms(164))
7) #5 NOT #6
8) #7 AND #2
9) #6 OR #8

Therapies for BPH:

Alcohol ablation of the prostate:

1) #9 AND (injections, intralesional(164) OR "chemo-ablation" OR chemoablation)
2) #9 AND (ethanol OR alcohol) AND (inject OR injection)
3) #9 AND sclerotherapy
4) #1 OR #2 OR #3

Balloon dilatation of the prostate (BDP):

1) #9 AND (balloon dilatation(164) OR (balloon AND dilat*) OR "BDP")

Cryotherapy:

1) #9 AND (cryotherapy OR cryotherapeutic OR cryosurgery OR cryosurgical OR hypotherm*)

High-intensity focused ultrasound (HIFU):

1) #9 AND (ultrasonic therapy OR ultrasound OR ultrasonic) AND (transrectal OR rectal OR endorectal)
2) #9 AND ("high-intensity focus ultrasound" OR "HIFU")
3) #9 AND sonoblate
4) #1 OR #2 OR #3
5) #4 AND (therapeutic use[sh] OR therapy[sh] OR publisher(222) OR premedline(222))

Laser surgery:

1) #9 AND (laser surgery(164) OR (laser AND (ablation OR interstitial OR holmium OR Endoscopic)) OR ELAP OR VLAP OR HoLEP OR HOLEP)

Open prostatectomy:

1) #9 AND prostatectomy AND (open OR invasive)

Prostatic stents:

1) #9 AND (stent* OR stents OR endoprosthes*)

Transurethral incision of the prostate (TUIP):

1) #9 AND ("Transurethral incision" OR "TUIP")

Transurethral microwave therapy (TUMT) of the prostate:

1) #9 AND (microwaves(164) OR microwave* OR "TUMT")

Transurethral needle ablation (TUNA) of the prostate:

1) #9 AND ("Transurethral needle ablation" OR (needle AND ablat*) OR radiofrequency OR "radio-frequency" OR "radio frequency" OR "RF" OR "TUNA")

Transurethral resection of the prostate (TURP):

1) #9 AND ("Transurethral resection" OR "TURP")

Transurethral vaporization of the prostate (TUVP):

1) #9 AND (electrovaporization OR "TUVP" OR vaporization OR "vapor-cut" OR rotoresection OR "TUVRP" OR rotoresect* OR gyrus OR wing)
2) #9 AND (electrocoagulation OR electrosurgery OR electrosurgical OR electrocautery OR loop)
3) #9 AND ("Transurethral evaporation" OR "TUEP")
4) #1 OR #2 OR #3

Watchful-waiting:

1) #9 AND ("watchful-waiting" OR "watchful waiting")
2) #9 AND ("untreated"[ab] OR "non-treatment")
3) #1 OR #2

Water-induced thermotherapy (WIT):

1) #9 AND (water[tw] OR water(164)) AND (Hyperthermia, induced(164) OR thermotherapy OR thermal*)
2) #9 AND thermoablation
3) #9 AND ("water-induced" OR "WIT")
4) #9 AND thermoflex
5) #9 AND ("hot-water" OR (hot AND water))
6) #2 OR #3 OR #4 OR #5

EMBASE searches

Below is the search strategy we used for EMBASE:

S1 s prostat?(2n)(hyperplasia or hypertrophy)

S2 s benign()prostatic()hyperplasia or bph

S3 s s1 or s2

S4 s s3 and py=1989:2003

S5 s s4/eng

S6 s s5/human

S7 s s6 and (urinary()tract()obstruction or prostatectomy of intermethod()comparison or transurethral()resection or laser()surgery or Transurethral()needle()ablation)

S8 s s6 and (TURP or TUIP or TUMT or TUNA or TUVP or TUEP or VLAP or HIFU or WIT)

S9 s s6 and (prostatectomy and Transurethral and resect?)

S10 s s6 and (microwaves/de or microwave)

S11 s s6 and (Transurethral()needle()ablation or (needle and ablat?) or radiofrequency or radio()frequency or rf)

S12 s s6 and (prostatectomy and (open or invasive or traditional))

S13 s s6 and (Transurethral and incision)

S14 s s6 and (Transurethral()resection or turp or tur)

S15 s s6 and (stent? Or stents/de)

S16 s s6 and (balloon dilatation/de or (balloon and dilatation))

S17 s s6 and (wit or water()induced or ((water/de or water) and (Hyperthermia, induced/de or thermoablation or thermotherapy or thermal?)))

S18 s s6 and (hifu or high()intensity()focus()ultrasound)

S19 s s6 and (laser surgery/de or (laser and (ablation or interstitial or holmium or Endoscopic)) or elap or vlap or holep or HoLEP)

S20	s s6 and (electrocoagulation or vaporization or electrosurgery or evaporation or electrosurgical or electrocautery or loop or vapor()cut or tuvrp or gyrus or wing or electrovaporization)
S21	s s6 and ((alcohol and ablat?) or chemoablat? Or sclerotherap? Or inject?))
S22	s s7 or s8 or s9 or s10 or s11 or s12 or s13 or s14 or s15 or s16 or s17 or s18 or s19 or s20 or s21
S23	s s22 and ((controlled study! Or clinical trial! Or randomization or cross-over procedure or double blind procedure or single blind procedure or placebo)/de or double()dummy or double()blind or single()blind or single()dummy)
S24	s s22 and (sham or random? Or placebo?)
S25	s s23 or s24
S26	s s25 not (letter or comment or editorial or news or case()report or notes or conference()paper)

Appendix D: Excluded Studies

Table D- 1. Excluded studies and reasons for exclusion

Study	Reason for exclusion
Schelin (2002)(249)	Evaluated the use of intraprostatic and periprostatic injections of mepivacaine epinephrine during TUMT; thus, did not evaluate TUMT itself
Isotalo (2001)(250)	All patients received a spiral stent and after two weeks were randomized to receive either finasteride or placebo. Thus, this was a comparison of finasteride, which is beyond the scope of this review.
Petas (2000)(195)	Both treatment groups received ILC, but one received a biodegradable stent after treatment. This study evaluates the post-treatment usefulness of a biodegradable stent rather than ILC or stenting as a treatment itself.
Wada (2000)(251)	Assigned patients to treatments based on prostate size, thus treatment groups were not comparable.
Djavan (1999b)(252)	Although this study evaluates two treatment groups receiving TUMT, the real comparison is between patients who received adjuvant alpha-blockade versus those who did not during their TUMT treatment.
Lukkarinen (1999)(253)	All patients received balloon dilation and were randomized into those who received finasteride or placebo. Thus, this was a comparison of finasteride, which is beyond the scope of this review.
Shalev (1999)(254)	This was a nonrandomized, retrospective comparison of acute myocardial infarction rates after TURP and open prostatectomy. The patients were assigned treatment on the basis of prostate size, and so were not matched.
Eliasson (1998)(255)	This was a comparison of results for helical coil TUMT versus filament TUMT. The results were stratified according to response, rather than according to treatment.
Devonec & Dahlstrand (1998)(256)	Both treatment groups received TUMT, but one received a temporary stent after TUMT. Evaluated temporary stenting after TUMT rather than TUMT itself.
Grundy (1997)(42)	All patients got TUEVP, but they were randomized to receive either sterile water or glycine as irrigation fluid. Thus, this was a comparison of irrigation fluids rather than different BPH treatments.
Horninger (1997)(257)	Study assigned patients to treatments based on general health or prostate volume. Thus, the comparison groups were not comparable.
Bdesha (1996)(258)	This was a comparison of TURP vs. open prostatectomy. Patients in one group had previously received TUMT, whereas patients in the other group had not. Thus, they were not comparable.

Table D- 1. Excluded studies and reasons for exclusion

Study	Reason for exclusion
De Wildt (1996)(259)	This study combined the results of Francisca et al. (1997)(171) and Ogden et al. (1993)(166) with longer followup time. However, there was an attrition rate of almost 50% after 3 months as patients were unblinded and given new treatment options. Thus, followup included only patients with successful treatment who did not seek additional treatment, which significantly biases results.
Te Slaa (1996)(260)	Study compared patients who received antibiotic prophylaxis for urinary tract infections (prior to BPH treatment) to patients who did not receive antibiotic prophylaxis. Therefore, it did not involve a comparison of treatments for BPH.
Abbou (1994)(258)	Results from patients receiving rectal hyperthermia and patients receiving urethral hyperthermia were combined.
Montorsi (1992)(187)	Transrectal hyperthermia. Treatment groups divided by age and thus not readily comparable.
Andersen (1990)(261)	This was a retrospective, nonrandomized comparison of mortality after TURP and open prostatectomy. The patients in the two groups were not matched and had different characteristics and disease severity.
Roos (1989)(262)	This was a retrospective, nonrandomized comparison of mortality and reoperation after TURP and open prostatectomy. The patients in the two groups were not matched and had different characteristics and disease severity.
Edwards (1982)(263)	This nonrandomized comparison of TUIP to TURP assigned treatment on the basis of prostate size, therefore the groups were not comparable.

Appendix E: Treatment Acronyms and Abbreviations in Text and Evidence Tables

Table E- 1. Description of acronyms and short phrases to denote treatments

Short phrase	Description
Balloon	Balloon dilation
CLAP	Contact laser ablation of the prostate
Cystoscopy	Insertion of endoscope, as control for balloon dilation
Expanding stent	Stent that expands once inserted
Fixed stent	Stent that does not expand once inserted
HIFU	High intensity focused ultrasound
HoLAP	Holmium laser ablation of the prostate
HoLRP	Holmium laser resection of the prostate
HoLEP	Holmium laser enucleation of the prostate
Hybrid laser	Hybrid laser technique
ILC	Interstitial laser coagulation
ILC with stent	Interstitial laser coagulation with stent
Medication	Treatment with medication only
No treatment	No treatment intervention or conservative management
Open prostX	Open prostatectomy
Sham	Imitation surgical procedure in which no prostate tissue is removed
Spiral stent	Spiral stent
Stent biodeg.	Temporary biodegradable stent
Temporary catheter	Temporary catheter, as control for temporary biodegradable stent
TRH 3-5x	Transrectal hyperthermia 3-5 applications
TRH 3-5x + meds	Transrectal hyperthermia 3-5 applications, with medication
TRH 6-10x	Transrectal hyperthermia 6-10 applications
TRH 6-10x + meds	Transrectal hyperthermia 6-10 applications, with medication
TRH 6-10x no cath.	Transrectal hyperthermia 6-10 applications, no catheterization
TUCT	Temporary urethral catheter (a form of sham treatment)
TUEVP	Transurethral electrovaporization of the prostate
TUIP	Transurethral incision of the prostate
TULIP	Transurethral ultrasound-guided laser incision of the prostate
TUMT	Transurethral microwave thermotherapy
TUMT 3 sessions	Transurethral microwave thermotherapy, 3 sessions
TUMT 30 min.	Transurethral microwave thermotherapy for 30 minutes
TUMT 6 sessions	Transurethral microwave thermotherapy, 6 sessions
TUMT high dose apex	Transurethral microwave thermotherapy, high dose, focused on the apex of the prostate

Table E- 1. Description of acronyms and short phrases to denote treatments

Short phrase	Description
TUMT high dose base	Transurethral microwave thermotherapy, high dose, focused on the base of the prostate
TUMT low dose apex	Transurethral microwave thermotherapy, low dose, focused on the apex of the prostate
TUNA	Transurethral needle ablation of the prostate
TUR syndrome	Transurethral resection syndrome
TURP	Transurethral resection of the prostate
TUT	Transurethral thermotherapy
VLAP	Visual laser ablation of the prostate
VLAP 1 catheter	Visual laser ablation of the prostate with one indwelling catheter
VLAP 2 catheters	Visual laser ablation of the prostate with indwelling and suprapubic catheters
VLAP DB	Visual laser ablation of the prostate with debridement
VLAP high power	Visual laser ablation of the prostate, high power
VLAP KTP	Visual laser ablation of the prostate using KTP fiber
VLAP low power	Visual laser ablation of the prostate, low power
VLAP painting	Visual laser ablation of the prostate, painting technique
VLAP with stent	Visual laser ablation of the prostate with stent
WIT	Water-induced thermotherapy

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Table E- 2. Abbreviations in Evidence Tables

Table type	Abbreviations
Study Details	N – No NC – Not calculable NR – Not reported Y – Yes Reported Outcomes: S – Symptoms T –Technical measures A – Adverse effects R – Retreatment Q – Quality of life P or Peri – Perioperative N enrolled – The number of patients enrolled in the two groups for this treatment comparison
Patient Inclusion Criteria	cc – cubic centimeters E – Patients were excluded for this characteristic g – grams I – Patients were included even if they had this characteristic IPSS – International Prostate Symptom Score (AUA) NR – Not reported PSA – Prostate specific antigen PVR (mL) – Postvoid Residual Volume in milliliters Qmax (mL/sec) – Maximum urinary flow rate in milliliters per second umol/L – Micromoles per liter UTI – Urinary tract infection
Treatment Details	Ch – Charr (equivalent to French) F or Fr – French (gauge measurement) KTP – Potassium titanyl phosphate yttrium-aluminum-garnet fiber MHz – Megahertz N – Number Nd:YAG – Neodymium:yttrium-aluminum-garnet fiber NR – Not reported tid – Three times daily W – Watt
Patient characteristics	I BO – Barosky irritative score Md – Median Mn – Mean N – Number of patients NR – Not reported O BO – Barosky obstructive score PSA – Prostate specific antigen PVR – Post-void residual volume SD – Standard deviation SE – Standard error of the mean

Table E- 2. Abbreviations in Evidence Tables

Table type	Abbreviations
Results and Change Comparisons	%chg – Percentage change from baseline %ile – Percentile 95% CI – 95% confidence interval Diff – Difference from baseline ICS – International Continence Society questionnaire IQR – Interquartile range md – Median mn – Mean N – Number of patients NR – Not reported NS – Not significant num pts – Number of patients Peri or P – Perioperative Post-op – Postoperative Q – Flow rate (quotient of volume/time) Ratio – Ratio of postoperative measure to baseline Rg – Range SD – Standard deviation SE – Standard error SEM – Standard error of the mean Sig. – Statistically significant SIR – Siroky maximum flow nomogram, expressed in standard deviation (SD) units.

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Appendix F: FDA Cleared or Approved Indications for Devices Used in BPH Treatments

The following information was retrieved by ECRI's database search staff, by querying FDA's PMA and 510k databases online at http://www.fda.gov/cdrh/. The information provided reflects all available information specific to BPH that was available through FDA. Note that many devices, particularly lasers, are FDA cleared for general indications, rather than for BPH specifically. If the cleared indications for a particular device did not mention BPH specifically, or was approved as a predicated device by the 510(k) process, we did not include information about that device in this table.

Table F- 1. FDA Regulation Status For BPH Treatment Devices

Treatment	Device (Manufacturer)	FDA approved/cleared urological indications	FDA approved/cleared contraindications
Laser procedures	CL MD Laser Systems (SLT)	CLAP – prostates up to 45 grams VLAP – prostates up to 75 grams	No details available
	Right Angle and Optilase Lasers (Trimedyne)	For coagulation of soft tissue for prostatectomy in the treatment of BPH (no further details available)	No details available
	Medilas D Laser family (Dornier Medtech)	>Age 50 Median and/or lateral lobes ranging from 28-85 cc	No details available
	Indigo® OPTIMA Laser System (Ethicon Endo-Surgery, Inc.)	Symptoms of BPH (Nothing more specific)	No details available

Treatment	Device (Manufacturer)	FDA approved/cleared urological indications	FDA approved/cleared contraindications
RFNA (TUNA®)	TUNA® (Medtronic)	Age >50 years Prostate size 20-50 cc Symptoms due to urinary flow obstruction secondary to BPH	Active UTI Neurogenic bladder Severe urethral stricture Bleeding disorders or patients taking anticoagulation medication unless antiplatelet meds have been discontinued for at least 10 days ASA Class group V patients Prostatic or bladder cancer Prostate gland <34 mm or >80 mm in transverse diameter Prosthetic device that may interfere with procedure Prostates previously treated with non-pharmacological therapies Presence of cardiac pacemaker, implantable defibrillator, or malleable penile implants Presence of implantable neurostimulation system.
HIFU	Sonablate® 500 System (Focus Surgery Inc.)	Not yet cleared by FDA	Not yet cleared by FDA
TUMT	Prostatron (Urologix)	Prostatron 2.0 (60 W max): Prostatic length of 35-50 mm Prostatron 2.5 (70 W max): Prostatic length of 25-50 mm Benefits of obstructive improvement outweigh the attendant risks	Peripheral artery disease with intermittent claudication Leriches syndrome Prostate or bladder cancer Severe urethral stricture Cardiac pacemaker, implantable defibrillator, or metallic implant in hip, pelvis, or femur.
	Targis (Urologix)	Prostatic length of 30-50 mm Prostatic urethra length of 25-35 mm	Prior pelvic radiation (Other contraindications do exist but full product labeling information was not available.)

Treatment	Device (Manufacturer)	FDA approved/cleared urological indications	FDA approved/cleared contraindications
TUMT	CoreTherm (Prostalund)	Prostate size of 30-100 g and length ≥35 mm	Severe urethral stricture Penile or urinary sphincter implants Previous radiation of pelvic region Bladder cancer Active prostatitis Active UTI Previous prostate or rectal surgery Wish to preserve fertility Implanted defibrillators, pacemakers, or other active implant Metallic implant in prostate treatment area Peripheral artery disease with inter
	TMX 2000 (Thermatrx)	Prostatic urethra length ≥30 mm Total prostate volume 30-100 cc Patients with bladder or prostate cancer CAN receive this treatment.	No details available.

Treatment	Device (Manufacturer)	FDA approved/cleared urological indications	FDA approved/cleared contraindications
	Prolieve™ System (Celsion)	Prostate size 20-80 grams Prostatic urethra length 1.2 cm – 5.5 cm Patients in whom drug therapy is typically indicated.	Patients whose pain has been relieved by any other treatment Severe urethral stricture Current urinary or prostatic infection Penile or urinary sphincter implant Peripheral artery disease with intermittent claudication Protruding middle lobe resulting in obstruction Evidence of prostate or bladder cancer Presence of metallic implants in pelvic region Presence of implanted cardiac pacemakers or defibrillators Previous transurethral prostatectomy Interest in preservation of fertility History of pelvic radiation Coagulation disorder Renal impairment Neurologic disorders affecting bladder function Bladder stones
Prostatic Stents	Urolume™ Endourethral Wallstent^{R} Prosthesis (American Medical Systems, Inc.)	To relieve prostatic obstruction secondary to benign prostatic hypertrophy (BPH) in men at least 60 years of age, or men under 60 years of age who are poor surgical candidates, and whose prostates are at least 2.5 cm in length	Fracture distraction defects of the posterior urethra; the device is not intended for temporary use
Water Induced Thermotherapy	Thermoflex™ WIT System (Argomed, Inc.)	>50 years old Symptoms of urinary obstruction Prostatic length 2.0-6.4 cm	No details available

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Alphabetical Bibliography

Abbou CC, Colombel M, Payan C, Beurton D, Viens-Bitker C, Richard F, Gibod LB, Leduc A, Jardin A, Chatelain C, et al.. The efficacy of microwave induced hyperthermia in the treatment of BPH: the Paris public hospitals' experience. Prog Clin Biol Res 1994;386:449-53.

Ackerman SJ, Rein AL, Blute M, Beusterien K, Sullivan EM, Tanio CP, Manyak MJ, Strauss MJ. Cost effectiveness of microwave thermotherapy in patients with benign prostatic hyperplasia: part I-methods. Urology 2000 Dec 20;56(6):972-80.

Ahmed M, Bell T, Lawrence WT, Ward JP, Watson GM. Transurethral microwave thermotherapy (Prostatron version 2.5) compared with transurethral resection of the prostate for the treatment of benign prostatic hyperplasia: a randomized, controlled, parallel study. Br J Urol 1997 Feb;79(2):181-5.

Albala DM, Turk TM, Fulmer BR, Koleski F, Andriole G, Davis BE, Eure GR, Kabalin JN, Lingeman J, Nuzzarello J, Sundaram C. Periurethral transurethral microwave thermotherapy for the treatment of benign prostatic hyperplasia: an interim 1-year safety and efficacy analysis using the thermatrx TMx-2000. Tech Urol 2000 Dec;6(4):288-93.

American Urological Association, AUA BPH Guideline Update Panel. Management of BPH (2003). Baltimore (MD): American Urological Association Education and Research, Inc.; 2003. 315 p. Also available: http://shop.auanet.org/timssnet/products/guidelines/bph_management.cfm.

Anderson TF, Bronnum-Hasen H, Sejr T, Roepstorff C. Elevated mortality following transurethral resection of the prostate for benign prostatic hypertrophy. But why? Med Care 1990;28:870-9.

Anson K, Nawrocki J, Buckley J, Fowler C, Kirby R, Lawrence W, Paterson P, Watson G. A multicenter, randomized, prospective study of endoscopic laser ablation versus transurethral resection of the prostate. Urology 1995 Sep;46(3):305-10.

Arai Y, Aoki Y, Okubo K, Maeda H, Terada N, Matsuta Y, Maekawa S, Ogura K. Impact of interventional therapy for benign prostatic hyperplasia on quality of life and sexual function: a prospective study. J Urol 2000 Oct;164(4):1206-11.

Armstrong K, Schwartz JS, Fitzgerald G, Putt M, Ubel PA. Effect of framing as gain versus loss on understanding and hypothetical treatment choices: survival and mortality curves. Med Decis Making 2002 Jan-Feb;22(1):76-83.

Arocho R, McMillan CA, Sutton-Wallace P. Construct validation of the USA-Spanish version of the SF-36 health survey in a Cuban-American population with benign prostatic hyperplasia. Qual Life Res 1998 Feb;7(2):121-6.

Barry MJ, Cockett AT, Holtgrewe HL, McConnell JD, Sihelnik SA, Winfield HN. Relationship of symptoms of prostatism to commonly used physiological and anatomical measures of the severity of benign prostatic hyperplasia. J Urol 1993 Aug 1;150(2):351-358.

Barry MJ, Fowler FJ Jr, O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK, Cockett AT. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. J Urol 1992 Nov;148(5):1549-57; discussion 1564.

Barry MJ, Fowler FJ Jr, O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK. Correlation of the American Urological Association symptom index with self-administered versions of the Madsen-Iversen, Boyarsky and Maine Medical Assessment Program symptom indexes. Measurement Committee of the American Urological Association. J Urol 1992 Nov;148(5):1558-63; discussion 1564.

Barry MJ, Mulley AG Jr, Fowler FJ, Wennberg JW. Watchful waiting vs immediate transurethral resection for symptomatic prostatism. The importance of patients' preferences. JAMA 1988 May 27;259(20):3010-7.

Barry MJ, Williford WO, Chang Y, Machi M, Jones KM, Walker-Corkery E, Lepor H. Benign prostatic hyperplasia specific health status measures in clinical research: how much change in the American Urological Association symptom index and the benign prostatic hyperplasia impact index is perceptible to patients? J Urol 1995 Nov;154(5):1770-4.

Barry MJ. Evaluation of symptoms and quality of life in men with benign prostatic hyperplasia. Urology 2001 Dec;58(6 Suppl 1):25-32; discussion 32.

Batista-Miranda JE, Diez MD, Bertran PA, Villavicencio H. Quality-of-life assessment in patients with benign prostatic hyperplasia: effects of various interventions. Pharmacoeconomics 2001;19(11):1079-90.

Bdesha AS, Bunce CJ, Kelleher JP, Snell ME, Vukusic J, Witherow RO. Transurethral microwave treatment for benign prostatic hypertrophy: a randomised controlled clinical trial. BMJ 1993 May 15;306(6888):1293-6.

Bdesha AS, Bunce CJ, Snell ME, Witherow RO. A sham controlled trial of transurethral microwave therapy with subsequent treatment of the control group. J Urol 1994 Aug;152(2 Pt 1):453-8.

Beerlage HP, Francisca EA, d'Ancona FC, Debruyne FM, De la Rosette JJ. Urolase v ultraline fibers in laser prostatectomy: 3-year follow-up of a randomized study. J Endourol 1998 Dec;12(6):575-80.

Bisonni RS, Lawler FH, Holtgrave DR. Transurethral prostatectomy versus transurethral dilatation of the prostatic urethra for benign prostatic hyperplasia: a cost-utility analysis. Fam Pract Res J 1993 Mar;13(1):25-36.

Bleichrodt H, Johannesson M. Standard gamble, time trade-off and rating scale: experimental results on the ranking properties of QALYs. J Health Econ 1997 Apr;16(2):155-75.

Blute M, Ackerman SJ, Rein AL, Beusterien K, Sullivan EM, Tanio CP, Strauss MJ, Manyak MJ. Cost effectiveness of microwave thermotherapy in patients with benign prostatic hyperplasia: part II--results. Urology 2000 Dec 20;56(6):981-7.

Blute ML, Patterson DE, Segura JW, Tomera KM, Hellerstein DK. Transurethral microwave thermotherapy v sham treatment: double-blind randomized study. J Endourol 1996 Dec;10(6):565-73.

Bolognese JA, Kozloff RC, Kunitz SC, Grino PB, Patrick DL, Stoner E. Validation of a symptoms questionnaire for benign prostatic hyperplasia. Prostate 1992;21(3):247-54.

Boon TA, Lepor H, Muschter R, McCullough DL. Laser treatment of benign prostatic hyperplasia (BPH) workshop. Prog Clin Biol Res 1994;386:535-44.

Borboroglu PG, Kane CJ, Ward JF, Roberts JL, Sands JP. Immediate and postoperative complications of transurethral prostatectomy in the 1990s. J Urol 1999 Oct;162(4):1307-10.

Bosch JL, Hop WC, Kirkels WJ, Schroder FH. The International Prostate Symptom Score in a community-based sample of men between 55 and 74 years of age: prevalence and correlation of symptoms with age, prostate volume, flow rate and residual urine volume. Br J Urol 1995 May;75(5):622-30.

Bosch JL. Urodynamic effects of various treatment modalities for benign prostatic hyperplasia. J Urol 1997 Dec;158(6):2034-44.

Boyarsky S, Jones G, Paulson DF. A new look at bladder neck obstruction by the Food and Drug Administration regulators: guidelines for investigation of benign prostatic hypertrophy. Trans Am Assoc Genitourin Surg 1977;68:29-32.

Brazier JE, Harper R, Jones NM, O'Cathain A, Thomas KJ, Usherwood T, Westlake L. Validating the SF-36 health survey questionnaire: new outcome measure for primary care. BMJ 1992 Jul 18;305(6846):160-4.

Breda G, Isgro A. Treatment of benign prostatic hyperplasia with water-induced thermotherapy: experience of a single institution. J Endourol 2002 Mar;16(2):123-6.

Brookes ST, Donovan JL, Peters TJ, Abrams P, Neal DE. Sexual dysfunction in men after treatment for lower urinary tract symptoms: evidence from randomised controlled trial. BMJ 2002 May 4;324(7345):1059-61.

Bruskewitz R, Issa MM, Roehrborn CG, Naslund MJ, Perez-Marrero R, Shumaker BP, Oesterling JE. A prospective, randomized 1-year clinical trial comparing transurethral needle ablation to transurethral resection of the prostate for the treatment of symptomatic benign prostatic hyperplasia. J Urol 1998 May;159(5):1588-93; discussion 1593-4.

Bryan NP, Hastie KJ, Chapple CR. Randomised prospective trial of contact laser prostatectomy (CLAP) versus visual laser coagulation of the prostate (VLAP) for the treatment of benign prostatic hyperplasia. 2-year follow-up. Eur Urol 2000 Sep;38(3):265-71.

Cabelin MA, Te AE, Kaplan SA. Transurethral vaporization of the prostate: current techniques. Curr Urol Rep 2000 Jul;1(2):116-23.

Carter A, Sells H, Speakman M, Ewings P, MacDonagh R, O'Boyle P. A prospective randomized controlled trial of hybrid laser treatment or transurethral resection of the prostate, with a 1-year follow-up. BJU Int 1999 Feb;83(3):254-9.

Carter A, Sells H, Speakman M, Ewings P, O'Boyle P, MacDonagh R. Quality of life changes following KTP/Nd:YAG laser treatment of the prostate and TURP. Eur Urol 1999 Aug;36(2):92-8.

CDRH 510(k) database search. [internet]. Rockville (MD): U.S. Food and Drug Administration (FDA), Center for Devices and Radiological Health (CDRH); [updated 2003 Sep 05]; [cited 2003 Sep 08]. Available: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm.

Center for Devices and Radiological Health (CDRH). FDA public health notification: serious injuries from microwave thermotherapy for benign prostatic hyperplasia. [internet]. Rockville (MD): U.S. Food and Drug Administration; 2000 Oct 11 [cited 2003 Jan 27]. [3 p]. Available: http://www.fda.gov/cdrh/safety.html.

Cetinkaya M, Ozturk B, Akdemir O, Aki FT. A comparison of fluid absorption during transurethral resection and transurethral vaporization for benign prostatic hyperplasia. BJU Int 2000 Nov;86(7):820-3.

Cetinkaya M, Ulusoy E, Adsan O, Saglam H, Ozturk B, Basay S. Comparative early results of transurethral electroresection and transurethral electrovaporization in benign prostatic hyperplasia. Br J Urol 1996 Dec;78(6):901-3.

Cetinkaya M, Ulusoy E, Ozturk B, Inal G, Memis A, Akdemir O. Transurethral resection or electrovaporization in the treatment of BPH. Br J Urol 1998 Apr;81(4):652-4.

Chacko KN, Donovan JL, Abrams P, Peters TJ, Brookes ST, Thorpe AC, Gujral S, Wright M, Kennedy LG, Neal DE. Transurethral prostatic resection or laser therapy for men with acute urinary retention: the CLasP randomized trial. J Urol 2001;166(1):166-70.

Chapple CR, Issa MM, Woo H. Transurethral needle ablation (TUNA®). A critical review of radiofrequency thermal therapy in the management of benign prostatic hyperplasia. Eur Urol 1999;35(2):119-28.

Chatelain C, Denis L, Foo KT, Khoury S, McConnell J, Abrams P, Barry M, Bartsch G, Boyle P, Brawer M, Corriere J, Debruyne F, Dreikorn K, Jardin A, Lee C, Naslund M, Nordling J, Resnick M, Roehrborn C. Recommendations of the International Scientific Committee: evaluation and treatment of lower urinary tract symptoms (LUTS) in older men. In: Proceedings of the fifth international consultation on BPH. Plymouth (UK): Health Publication Ltd.; 2001. p. 519-34.

Cher DJ, Miyamoto J, Lenert LA. Incorporating risk attitude into Markov-process decision models: importance for individual decision making. Med Dec Making 1997 Jul-Sep;17(3):340-50.

Christensen MM, Aagaard J, Madsen PO. Transurethral resection versus transurethral incision of the prostate. A prospective randomized study. Urol Clin North Am 1990 Aug;17(3):621-30.

Cooper EC. Methodological issues in AIDS clinical trials. Active control equivalence trials. J Acquir Immune Defic Syndr 1990;3 Suppl 2:S77-81.

Costello AJ, Crowe HR, Jackson T, Street A. A randomised single institution study comparing laser prostatectomy and transurethral resection of the prostate. Ann Acad Med Singapore 1995 Sep;24(5):700-4.

Cowles RS 3d, Kabalin JN, Childs S, Lepor H, Dixon C, Stein B, Zabbo A. A prospective randomized comparison of transurethral resection to visual laser ablation of the prostate for the treatment of benign prostatic hyperplasia. Urology 1995 Aug;46(2):155-60.

Cranovsky R, Matillon Y, Banta D. EUR-ASSESS project subgroup report on coverage. Int J Technol Assess Health Care 1997 Spring;13(2):287-332.

D'Agostino RB Sr, Massaro JM, Sullivan LM. Non-inferiority trials: design concepts and issues - the encounters of academic consultants in statistics. Stat Med 2003 Jan;22(2):169-86.

D'Agostino RB Sr. Non-inferiority trials: advances in concepts and methodology. Stat Med 2003 Jan;22(2):165-7.

Dahlstrand C, Walden M, Geirsson G, Pettersson S. Transurethral microwave thermotherapy versus transurethral resection for symptomatic benign prostatic obstruction: a prospective randomized study with a 2-year follow-up. Br J Urol 1995 Nov;76(5):614-8.

D'Ancona CA, Netto NR Junior, Cara AM, Ikari O. Internal urethrotomy of the prostatic urethra or transurethral resection in benign prostatic hyperplasia. J Urol 1990 Oct;144(4):918-20.

D'Ancona FC, Francisca EA, Witjes WP, Welling L, Debruyne FM, De La Rosette JJ. Transurethral resection of the prostate vs high-energy thermotherapy of the prostate in patients with benign prostatic hyperplasia: long-term results. Br J Urol 1998 Feb;81(2):259-64.

D'Ancona FC, Francisca EA, Witjes WP, Welling L, Debruyne FM, de la Rosette JJ. High energy thermotherapy versus transurethral resection in the treatment of benign prostatic hyperplasia: results of a prospective randomized study with 1 year of followup. J Urol 1997 Jul;158(1):120-5.

de la Rosette J. Laser therapy: to combine the best of the new with the best of the old. J Urol (Paris) 1995;101(1):37-9.

de la Rosette JJ, Alivizatos G, Laguna MP. Transurethral hot water balloon thermoablation. Curr Urol Rep 2001 Aug;2(4):302-5.

de la Rosette JJ, Alivizatos G, Madersbacher S, Perachino M, Thomas D, Desgrandchamps F, de Wildt M. EAU Guidelines on benign prostatic hyperplasia (BPH). Eur Urol 2001 Sep;40(3):256-63; discussion 264.

de la Rosette JJ, te Slaa E, de Wildt MJ, Debruyne FM. Experience with the Ultraline and Urolase laser fibers: is there any difference. World J Urol 1995;13(2):98-103.

de Wildt MJ, Hubregtse M, Ogden C, Carter SS, Debruyne FM, De la Rosette JJ. A 12-month study of the placebo effect in transurethral microwave thermotherapy. Br J Urol 1996 Feb;77(2):221-7.

Debruyne FM, Djavan B, De la Rosette J, Desgrandchamps F, Fourcade R, Gibbon R, Kaplan S, Hartung R, Krane R, Manyak M, Mebust W, Muschter R, Murai M, Schulman CC, Sedelaar JP, Stein B, Teillac P, Zlotta A. Interventional therapy for benign prostatic hyperplasia. In: Proceedings of the fifth international consultation on BPH. Plymouth (UK): Health Publication Ltd.; 2001. p. 399-421.

Deckert T, Yokoyama H, Mathiesen E, Ronn B, Jensen T, Feldt-Rasmussen B, Borch-Johnsen K, Jensen JS. Cohort study of predictive value of urinary albumin excretion for atherosclerotic vascular disease in patients with insulin dependent diabetes. BMJ 1996 Apr 6;312(7035):871-4.

Devonec M, Dahlstrand C. Temporary urethral stenting after high-energy transurethral microwave thermotherapy of the prostate. World J Urol 1998;16(2):120-3.

Diagnostic and therapeutic technology assessment. Endoscopic balloon dilation of the prostate. JAMA 1992 Feb 26;267(8):1123-4, 1127-8.

Dimberg M, Norlen H, Allgen LG, Allgen T, Wallin M. A comparison between two hypotonic irrigating solutions used in transurethral resections of the prostate: sorbitol (2%)-mannitol (1%) and 1.5% glycine solutions. Scand J Urol Nephrol 1992;26(3):241-7.

Ditrolio J, Patel P, Watson RA, Irwin RJ. Chemo-ablation of the prostate with dehydrated alcohol for the treatment of prostatic obstruction. J Urol 2002 May;167(5):2100-3; discussion 2103-4.

Djavan B, Seitz C, Roehrborn CG, Remzi M, Fakhari M, Waldert M, Basharkhah A, Planz B, Harik M, Marberger M. Targeted transurethral microwave thermotherapy versus alpha-blockade in benign prostatic hyperplasia: outcomes at 18 months. Urology 2001 Jan;57(1):66-70.

Djavan B, Shariat S, Fakhari M, Ghawidel K, Seitz C, Partin AW, Roehrborn CG, Marberger M. Neoadjuvant and adjuvant alpha-blockade improves early results of high- energy transurethral microwave thermotherapy for lower urinary tract symptoms of benign prostatic hyperplasia: a randomized, prospective clinical trial. Urology 1999 Feb;53(2):251-9.

Djavan B. Benign prostatic hyperplasia: where do we stand in the new millennium? Curr Opin Urol 2002;12:1-2.

Dolan P, Gudex C. Time preference, duration and health state valuations. Health Econ 1995 Jul-Aug;4(4):289-99.

Doll HA, Black NA, Flood AB, McPherson K. Criterion validation of the Nottingham Health Profile: patient views of surgery for benign prostatic hypertrophy. Soc Sci Med 1993 Jul;37(1):115-22.

Donnelly V, Foran A, Murphy J, McParland P, Keane D, O'Herlihy C. Neonatal brachial plexus palsy: an unpredictable injury. Am J Obstet Gynecol 2002 Nov;187(5):1209-12.

Donovan JL, Abrams P, Peters TJ, Kay HE, Reynard J, Chapple C, De La Rosette JJ, Kondo A. The ICS-'BPH' Study: the psychometric validity and reliability of the ICSmale questionnaire. Br J Urol 1996 Apr;77(4):554-62.

Donovan JL, Peters TJ, Abrams P, Brookes ST, de aa Rosette JJ, Schafer W. Scoring the short form ICSmaleSF questionnaire. International Continence Society. J Urol 2000 Dec;164(6):1948-55.

Donovan JL, Peters TJ, Neal DE, Brookes ST, Gujral S, Chacko KN, Wright M, Kennedy LG, Abrams P. A randomized trial comparing transurethral resection of the prostate, laser therapy and conservative treatment of men with symptoms associated with benign prostatic enlargement: The CLasP study. J Urol 2000 Jul;164(1):65-70.

Dorflinger T, Jensen FS, Krarup T, Walter S. Transurethral prostatectomy compared with incision of the prostate in the treatment of prostatism caused by small benign prostate glands. Scand J Urol Nephrol 1992;26(4):333-8.

Dorflinger T, Oster M, Larsen JF, Walter S, Krarup T. Transurethral prostatectomy or incision of the prostate in the treatment of prostatism caused by small benign prostates. Scand J Urol Nephrol Suppl 1987;104:77-81.

Dull P, Reagan RW Jr, Bahnson RR. Managing benign prostatic hyperplasia. Am Fam Physician 2002 Jul 1;66(1):77-84.

Edwards L, Powell C. An objective comparison of transurethral resection and bladder neck incision in the treatment of prostatic hypertrophy. J Urol 1982 Aug;128(2):325-7.

Ekengren J, Haendler L, Hahn RG. Clinical outcome 1 year after transurethral vaporization and resection of the prostate. Urology 2000 Feb;55(2):231-5.

Eliasson T, Terio H, Damber JE. Transurethral microwave thermotherapy for benign prostatic hyperplasia--experience with the Prostcare. World J Urol 1998;16(2):109-14.

Epstein RS, Deverka PA, Chute CG, Panser L, Oesterling JE, Lieber MM, Schwartz S, Patrick D. Validation of a new quality of life questionnaire for benign prostatic hyperplasia. J Clin Epidemiol 1992 Dec;45(12):1431-45.

Erdagi U, Akman RY, Sargin SY, Yazicioglu A. Transurethral electrovaporization of the prostate versus transurethral resection of the prostate: a prospective randomized study. Arch Ital Urol Androl 1999 Jun;71(3):125-30.

Fenter TC. (American Urological Association). Personal communication. 2004 Mar 4.

Fitzpatrick JM, Kasidas GP, Rose GA. Hyperoxaluria following glycine irrigation for transurethral prostatectomy. Br J Urol 1981 Jun;53(3):250-2.

Floratos DL, Kiemeney LA, Rossi C, Kortmann BB, Debruyne FM, de La Rosette JJ. Long-term followup of randomized transurethral microwave thermotherapy versus transurethral prostatic resection study. J Urol 2001 May;165(5):1533-8.

Focus Surgery. Noninvasive therapy for prostate diseases: Focus surgery has positive prostate cancer results using high intensity focused ultrasound (HIFU). [internet]. Indianapolis (IN): Focus Surgery, Inc.; 2003 [cited 2003 Sep 09]. [2 p]. Available: http://www.focus-surgery.com.

Fowler FJ Jr, Wennberg JE, Timothy RP, Barry MJ, Mulley AG Jr, Hanley D. Symptom status and quality of life following prostatectomy. JAMA 1988 May 27;259(20):3018-22.

Francisca EA, d'Ancona FC, Hendriks JC, Kiemeney LA, Debruyne FM, de la Rosette JJ. Quality of life assessment in patients treated with lower energy thermotherapy (Prostasoft 2.0): results of a randomized transurethral microwave thermotherapy versus sham study. J Urol 1997 Nov;158(5):1839-44.

Francisca EA, d'Ancona FC, Hendriks JC, Kiemeney LA, Debruyne FM, de La Rosette JJ. A randomized study comparing high-energy TUMT to TURP: quality-of-life results. Eur Urol 2000 Nov;38(5):569-75.

Francisca EA, d'Ancona FC, Meuleman EJ, Debruyne FM, de la Rosette JJ. Sexual function following high energy microwave thermotherapy: results of a randomized controlled study comparing transurethral microwave thermotherapy to transurethral prostatic resection. J Urol 1999 Feb;161(2):486-90.

Fraundorfer MR, Gilling PJ, Kennett KM, Dunton NG. Holmium laser resection of the prostate is more cost effective than transurethral resection of the prostate: results of a randomized prospective study. Urology 2001 Mar;57(3):454-8.

Gallucci M, Puppo P, Perachino M, Fortunato P, Muto G, Breda G, Mandressi A, Comeri G, Boccafoschi C, Francesca F, Guazzieri S, Pappagallo GL. Transurethral electrovaporization of the prostate vs. transurethral resection. Results of a multicentric, randomized clinical study on 150 patients. Eur Urol 1998;33(4):359-64.

Giannakopoulos X, Grammeniatis E, Gartzios A, et al. Transurethral needle ablation (TUNA) of the prostate: preliminary results using the new generation TUNA III catheter on patients with symptomatic BPH controlled by a series of 50 patients using TUNA II device. Eur Urol 1996;30:986.

Gilling PJ, Cass CB, Malcolm A, Cresswell M, Fraundorfer MR, Kabalin JN. Holmium laser resection of the prostate versus neodymium:yttrium-aluminum-garnet visual laser ablation of the prostate: a randomized prospective comparison of two techniques for laser prostatectomy. Urology 1998 Apr;51(4):573-7.

Gilling PJ, Cass CB, Malcolm AR, Fraundorfer MR. Combination holmium and Nd:YAG laser ablation of the prostate: initial clinical experience. J Endourol 1995 Apr;9(2):151-3.

Gilling PJ, Kennett KM, Fraundorfer MR. Holmium laser resection v transurethral resection of the prostate: results of a randomized trial with 2 years of follow-up. J Endourol 2000 Nov;14(9):757-60.

Gilling PJ, Mackey M, Cresswell M, Kennett K, Kabalin JN, Fraundorfer MR. Holmium laser versus transurethral resection of the prostate: a randomized prospective trial with 1-year followup. J Urol 1999 Nov;162(5):1640-4.

Girman CJ, Jacobsen SJ, Rhodes T, Guess HA, Roberts RO, Lieber MM. Association of health-related quality of life and benign prostatic enlargement. Eur Urol 1999 Apr;35(4):277-84.

Gotoh M, Okamura K, Hattori R, Nishiyama N, Kobayashi H, Tanaka K, Yamada S, Kato T, Kinukawa T, Ono Y, Ohshima S. A randomized comparative study of the Bandloop versus the standard loop for transurethral resection of the prostate. J Urol 1999 Nov;162(5):1645-7.

Greene WL, Concato J, Feinstein AR. Claims of equivalence in medical research: are they suppored by the evidence. Ann Intern Med 2000 May;132(9):715-22.

Grundy PL, Budd DW, England R. A randomized controlled trial evaluating the use of sterile water as an irrigation fluid during transurethral electrovaporization of the prostate. Br J Urol 1997 Dec;80(6):894-7.

Gujral S, Abrams P, Donovan JL, Neal DE, Brookes ST, Chacko KN, Wright MJ, Timoney AG, Peters TJ. A prospective randomized trial comparing transurethral resection of the prostate and laser therapy in men with chronic urinary retention: The CLasP study. J Urol 2000 Jul;164(1):59-64.

Hahn RG, Nilsson A, Farahmand BY, Ekengren J, Persson PG. Operative factors and the long-term incidence of acute myocardial infarction after transurethral resection of the prostate. Epidemiology 1996 Jan;7(1):93-5.

Haines SJ, Walters BC. Proof of equivalence. The inference of statistical significance. Caveat emptor [editorial]. Neurosurgery 1993 Sep;33(3):432-3.

Hammadeh MY, Fowlis GA, Singh M, Philp T. Transurethral electrovaporization of the prostate--a possible alternative to transurethral resection: a one-year follow-up of a prospective randomized trial. Br J Urol 1998 May;81(5):721-5.

Hammadeh MY, Madaan S, Singh M, Philp T. A 3-year follow-up of a prospective randomized trial comparing transurethral electrovaporization of the prostate with standard transurethral prostatectomy. BJU Int 2000 Oct;86(6):648-51.

Hammadeh MY, Madaan S, Singh M, Philp T. Two-year follow-up of a prospective randomised trial of electrovaporization versus resection of prostate. Eur Urol 1998 Sep;34(3):188-92.

Hansen BJ, Flyger H, Brasso K, Schou J, Nordling J, Thorup Andersen J, Mortensen S, Meyhoff HH, Walter S, Hald T. Validation of the self-administered Danish Prostatic Symptom Score (DAN-PSS-1) system for use in benign prostatic hyperplasia. Br J Urol 1995 Oct;76(4):451-8.

Hansen BJ, Mortensen S, Mensink HJ, Flyger H, Riehmann M, Hendolin N, Nordling J, Hald T. Comparison of the Danish Prostatic Symptom Score with the International Prostatic Symptom Score, the Madsen-Iversen and Boyarsky symptom indexes. ALFECH Study Group. Br J Urol 1998 Jan;81(1):36-41.

Hansen MV, Zdanowski A. The use of a simple home flow test as a quality indicator for male patients treated for lower urinary tract symptoms suggestive of bladder outlet obstruction. Eur Urol 1997;32(1):34-8.

Heaton JP. Radiofrequency thermal ablation of the prostate: the TUNA technique. Tech Urol 1995 Spring;1(1):3-10.

Helke C, Manseck A, Hakenberg OW, Wirth MP. Is transurethral vaporesection of the prostate better than standard transurethral resection. Eur Urol 2001 May;39(5):551-7.

Hellstrom P, Lukkarinen O, Kontturi M. Bladder neck incision or transurethral electroresection for the treatment of urinary obstruction caused by a small benign prostate? A randomized urodynamic study. Scand J Urol Nephrol 1986;20(3):187-92.

Hettiarachchi JA, Samadi AA, Konno S, Das AK. Holmium laser enucleation for large (greater than 100 mL) prostate glands. Int J Urol 2002 May;9(5):233-6.

Hill B, Belville W, Bruskewitz R, Issa M, Perez-Marrero R, Roehrborn C, Terris M, Naslund M. Transurethral needle ablation versus transurethral resection of the prostate for the treatment of symptomatic benign prostatic hyperplasia: 5-year results of a prospective, randomized, multicenter clinical trial. J Urol 2004 Jun;171(6 Pt 1):2336-40.

Hoekstra PT, Kahnoski R, McCamish MA, Bergen W, Heetderks DR. Transurethral prostatic resection syndrome--a new perspective: encephalopathy with associated hyperammonemia. J Urol 1983 Oct;130(4):704-7.

Holtgrewe HL, Mebust WK, Dowd JB, Cockett AT, Peters PC, Proctor C. Transurethral prostatectomy: practice aspects of the dominant operation in American urology. J Urol 1989 Feb;141(2):248-53.

Holtgrewe HL. Transurethral prostatectomy. Urol Clin North Am 1995 May;22(2):357-68.

Horninger W, Janetschek G, Watson G, Reissigl A, Strasser H, Bartsch G. Are contact laser, interstitial laser, and transurethral ultrasound-guided laser-induced prostatectomy superior to transurethral prostatectomy. Prostate 1997 Jun 1;31(4):255-63.

Horninger W, Unterlechner H, Strasser H, Bartsch G. Transurethral prostatectomy: mortality and morbidity. Prostate 1996 Mar;28(3):195-200.

Hung HM, Wang SJ, Tsong Y, Lawrence J, O'Neil RT. Some fundamental issues with non-inferiority testing in active controlled trials. Stat Med 2003 Jan;22(2):213-25.

Isotalo T, Talja M, Hellstrom P, Perttila I, Valimaa T, Tormala P, Tammela TL. A double-blind, randomized, placebo-controlled pilot study to investigate the effects of finasteride combined with a biodegradable self-reinforced poly L-lactic acid spiral stent in patients with urinary retention caused by bladder outlet [truncated]. BJU Int 2001 Jul;88(1):30-4.

Issa MM, Myrick SE, Symbas NP. The TUNA procedure for BPH: review of technology. Infect Urol 1998;11(4):104-11. Also available: http://www.medscape.com/SCP/IIU/1998/v11.n04/u3086.issa/pnt-u3086.issa.html.

Jahnson S, Dalen M, Gustavsson G, Pedersen J. Transurethral incision versus resection of the prostate for small to medium benign prostatic hyperplasia. Br J Urol 1998 Feb;81(2):276-81.

Jenkinson C, Gray A, Doll H, Lawrence K, Keoghane S, Layte R. Evaluation of index and profile measures of health status in a randomized controlled trial. Comparison of the medical outcomes study 36-item short form health survey, EuroQol, and disease specific measures. Med Care 1997 Nov;35(11):1109-18.

Jung P, Mattelaer P, Wolff JM, Mersdorf A, Jakse G. Visual laser ablation of the prostate: efficacy evaluated by urodynamics and compared to TURP. Eur Urol 1996;30(4):418-23.

Kabalin JN, Gill HS, Bite G, Wolfe V. Comparative study of laser versus electrocautery prostatic resection: 18-month followup with complex urodynamic assessment. J Urol 1995 Jan;153(1):94-7; discussion 97-8.

Kabalin JN. Laser prostatectomy performed with a right angle firing neodymium:YAG laser fiber at 40 watts power setting. J Urol 1993 Jul;150(1):95-9.

Kaplan SA, Laor E, Fatal M, Te AE. Transurethral resection of the prostate versus transurethral electrovaporization of the prostate: a blinded, prospective comparative study with 1-year followup. J Urol 1998 Feb;159(2):454-8.

Keoghane SR, Cranston DW, Lawrence KC, Doll HA, Fellows GJ, Smith JC. The Oxford Laser Prostate Trial: a double-blind randomized controlled trial of contact vaporization of the prostate against transurethral resection; preliminary results. Br J Urol 1996 Mar;77(3):382-5.

Keoghane SR, Doll HA, Lawrence KC, Jenkinson CP, Cranston DW. The Oxford Laser Prostate Trial: sexual function data from a randomized controlled clinical trial of contact laser prostatectomy. Eur Urol 1996;30(4):424-8.

Keoghane SR, Lawrence KC, Gray AM, Doll HA, Hancock AM, Turner K, Sullivan ME, Dyar O, Cranston D. A double-blind randomized controlled trial and economic evaluation of transurethral resection vs contact laser vaporization for benign prostatic enlargement: a 3-year follow-up. BJU Int 2000 Jan;85(1):74-8.

Keoghane SR, Lawrence KC, Jenkinson CP, Doll HA, Chappel DB, Cranston DW. The Oxford Laser Prostate Trial: sensitivity to change of three measures of outcome. Urology 1996 Jan;47(1):43-7.

Kitagawa M, Furuse H, Fukuta K, Aso Y. Holmium:YAG laser resection of the prostate versus visual laser ablation of the prostate and transurethral ultrasound-guided laser induced prostatectomy: a retrospective comparative study. Int J Urol 1998 Mar;5(2):152-6.

Krongrad A, Granville LJ, Burke MA, Golden RM, Lai S, Cho L, Niederberger CS. Predictors of general quality of life in patients with benign prostate hyperplasia or prostate cancer. J Urol 1997 Feb;157(2):534-8.

Krumins PE, Fihn SD, Kent DL. Symptom severity and patients' values in the decision to perform a transurethral resection of the prostate. Med Decis Making 1988 Jan-Mar;8(1):1-8.

Kuntz RM, Lehrich K. Transurethral holmium laser enucleation versus transvesical open enucleation for prostate adenoma greater than 100 gm.: a randomized prospective trial of 120 patients. J Urol 2002 Oct;168(4 Pt 1):1465-9.

Kupeli B, Yalcinkaya F, Topaloglu H, Karabacak O, Gunlusoy B, Unal S. Efficacy of transurethral electrovaporization of the prostate with respect to standard transurethral resection. J Endourol 1998 Dec;12(6):591-4.

Kupeli S, Yilmaz E, Soygur T, Budak M. Randomized study of transurethral resection of the prostate and combined transurethral resection and vaporization of the prostate as a therapeutic alternative in men with benign prostatic hyperplasia. J Endourol 2001 Apr;15(3):317-21.

Kursh ED, Concepcion R, Chan S, Hudson P, Ratner M, Eyre R. Interstitial laser coagulation versus transurethral prostate resection for treating benign prostatic obstruction: a randomized trial with 2-year follow-up. Urology 2003 Mar;61(3):573-8.

Laduc R. Thermotherapy. Results of a prospective, randomized, double blind, placebo controlled study. In: Laduc R, Weil EH, Zerbib M, Perrin P, Denis L. Thermotherapy and hyperthermia workshop. Prog Clin Biol Res 1994;386:487-98.

Lam JS, Volpe MA, Kaplan SA. Use of prostatic stents for the treatment of benign prostatic hyperplasia in high-risk patients. Curr Urol Rep 2001 Aug;2(4):277-84.

Larsen EH, Dorflinger T, Gasser C, Graversen PH, Bruskewitz RC. Transurethral incision versus transurethral resection of the prostate for treatment of benign prostatic hypertrophy, a preliminary report. Scand J Urol Nephrol 1987;21(suppl 104):83-6.

Larson TR, Blute ML, Bruskewitz RC, Mayer RD, Ugarte RR, Utz WJ. A high-efficiency microwave thermoablation system for the treatment of benign prostatic hyperplasia: results of a randomized, sham-controlled, prospective, double-blind, multicenter clinical trial. Urology 1998 May;51(5):731-42.

Larson TR, Blute ML, Tri JL, Whitlock SV. Contrasting heating patterns and efficiency of the Prostatron and Targis microwave antennae for thermal treatment of benign prostatic hyperplasia. Urology 1998 Jun;51(6):908-15.

Lenert LA, Ziegler J, Lee T, Unfred C, Mahmoud R. The risks of multimedia methods: effects of actor's race and gender on preferences for health states. J Am Med Inform Assoc 2000 Mar-Apr;7(2):177-85.

Li MK, Ng AS. Bladder neck resection and transurethral resection of the prostate: a randomized prospective trial. J Urol 1987 Oct;138(4):807-9.

Lindner A, Braf Z, Lev A, Golomb J, Leib Z, Siegel Y, Servadio C. Local hyperthermia of the prostate gland for the treatment of benign prostatic hypertrophy and urinary retention. Br J Urol 1990 Feb;65(2):201-3.

Lingeman J. Thermotherapy evolves beyond cooling: the logic behind the next generation devices. [internet]. Northbrook (IL): Thermatrx; 2002 [cited 2003 Sep 02]. [2 p]. Available: http://www.thermatrx.com.

Littlejohn JO Jr, Ghafar MA, Kang YM, Kaplan SA. Transurethral resection of the prostate: the new old standard. Curr Opin Urol 2002 Jan;12(1):19-23.

Llewellyn-Thomas HA, Williams JI, Levy L, Naylor CD. Using a trade-off technique to assess patients' treatment preferences for benign prostatic hyperplasia. Med Decis Making 1996 Jul-Sep;16(3):262-82.

Lukacs B, Comet D, Grange JC, Thibault P. Construction and validation of a short-form benign prostatic hypertrophy health-related quality-of-life questionnaire. BPH Group in General Practice. Br J Urol 1997 Nov;80(5):722-30.

Lukkarinen O, Lehtonen T, Talja M, Lundstedt S, Tiitinen J, Taari K. Finasteride following balloon dilatation of the prostate. A double-blind, placebo-controlled, multicenter study. Ann Chir Gynaecol 1999;88(4):299-303.

MacDiarmid SA, Goodson TC, Holmes TM, Martin PR, Doyle RB. An assessment of the comprehension of the American Urological Association Symptom Index. J Urol 1998 Mar;159(3):873-4.

MacDonagh RP, Cliff AM, Speakman MJ, O'Boyle PJ, Ewings P, Gudex C. The use of generic measures of health-related quality of life in the assessment of outcome from transurethral resection of the prostate. Br J Urol 1997 Mar;79(3):401-8.

Madersbacher S, Djavan B, Marberger M. Minimally invasive treatment for benign prostatic hyperplasia. Curr Opin Urol 1998;8:17-26.

Madersbacher S, Marberger M. Is transurethral resection of the prostate still justified? BJU Int 1999 Feb;83(3):227-37.

Madsen PO, Iversen P. A point system for selecting operative candidates. In: Hinman F Jr, editors. Benign prostatic hypertrophy. New York: Springer-Verlag; 1983. p. 763-5.

Makuch R, Johnson M. Issues in planning and interpreting active control equivalence studies. J Clin Epidemiol 1989;42(6):503-11.

Malek RS, Hai MA, Nseyo UO, Lapeyrolerie J. Photoselective vaporization of the prostate: breakthrough treatment for BPH. Urol Times 2002 May;30(Suppl 1):4-20.

Manyak MJ, Ackerman SJ, Blute ML, Rein AL, Buesterien K, Sullivan EM, Tanio CP, Strauss MJ. Cost effectiveness of treatment for benign prostatic hyperplasia: an economic model for comparison of medical, minimally invasive, and surgical therapy. J Endourol 2002 Feb;16(1):51-6.

Martenson AC, De la Rosette JJMCH. Interstitial laser coagulation in the treatment of benign prostatic hyperplasia using a diode laser system: results of an evolving technology. Prostate Cancer Prostatic Dis 1999;2(3):148-54.

May F, Guenther M, Fastenmeier K, Hartung R. Improved high-frequency surgery for transurethral resection of the prostate: report from a multicenter trial and identification of risk groups [abstract ID: 101757]. In: 2003 AUA annual meeting; 2003 Apr 26-May 1; Chicago (IL). Baltimore (MD): American Urological Association; 2003. Also available: http://aua03.agora.com/planner/displayabstract.asp?presentationid=1729.

McHorney CA. Generic health measurement: past accomplishments and a measurement paradigm for the 21st century. Ann Intern Med 1997 Oct 15;127(8 Pt 2):743-50.

Mebust WK, Holtgrewe HL, Cockett AT, Peters PC. Transurethral prostatectomy: immediate and postoperative complications. A cooperative study of 13 participating institutions evaluating 3,885 patients. J Urol 1989 Feb;141(2):243-7.

Meeting transcript. Cardiovascular and Renal Drugs Advisory Committee 82nd Meeting. 1997 Oct 23; Bethesda (MD). Rockville (MD): U.S. Food and Drug Administration; 1997 Oct 23. 161 p. Also available: http://www.fda.gov/ohrms/dockets/ac/97/transcpt/3338t1.pdf.

Meyhoff HH, Nordling J, Hald T. Urodynamic evaluation of transurethral versus transvesical prostatectomy. A randomized study. Scand J Urol Nephrol 1984;18(1):27-35.

Meyhoff HH. Transurethral versus transvesical prostatectomy. Clinical, urodynamic, renographic and economic aspects. A randomized study. Scand J Urol Nephrol Suppl 1987;102:1-26.

Montie JE, Tremper K. Anesthesia requirements during transurethral needle ablation procedure [letter; comment]. Urology 1998 Jul;52(1):158.

Montorsi F, Galli L, Guazzoni G, Colombo R, Bulfamante G, Barbieri L, Matozzo V, Grazioli V, Rigatti P. Transrectal microwave hyperthermia for benign prostatic hyperplasia: long-term clinical, pathological and ultrastructural patterns. J Urol 1992 Aug;148(2 Pt 1):321-5.

Montorsi F, Guazzoni G, Bergamaschi F, Consonni P, Galli L, Rigatti P. A comparison of transrectal hyperthermia, transurethral thermotherapy, urolume wallstent, and prostatic spiral for benign prostatic hyperplasia patients at poor operative risk. Prostate 1994;24(3):156-61.

Moody JA, Lingeman JE. Holmium laser enucleation for prostate adenoma greater than 100 gm.: comparison to open prostatectomy. J Urol 2001 Feb;165(2):459-62.

Morrow GR, Lindke J, Black P. Measurement of quality of life in patients: psychometric analyses of the Functional Living Index-Cancer (FLIC). Qual Life Res 1992 Oct;1(5):287-96.

Mostafid AH, Harrison NW, Thomas PJ, Fletcher MS. A prospective randomized trial of interstitial radiofrequency therapy versus transurethral resection for the treatment of benign prostatic hyperplasia. Br J Urol 1997 Jul;80(1):116-22.

Mottet N, Anidjar M, Bourdon O, Louis JF, Teillac P, Costa P, Le Duc A. Randomized comparison of transurethral electroresection and Holmium:YAG laser vaporization for symptomatic benign prostatic hyperplasia. J Endourol 1999 Mar;13(2):127-30.

Mulvin D, Creagh T, Kelly D, Smith J, Quinlan D, Fitzpatrick J. Transurethral microwave thermotherapy versus transurethral catheter therapy for benign prostatic hyperplasia. Eur Urol 1994;26(1):6-9.

Muschter R. Interstitial laser therapy. Curr Opin Urol 1996;6:33-8.

Narayan P, Tewari A, Aboseif S, Evans C. A randomized study comparing visual laser ablation and transurethral evaporation of prostate in the management of benign prostatic hyperplasia. J Urol 1995 Dec;154(6):2083-8.

Nawrocki JD, Bell TJ, Lawrence WT, Ward JP. A randomized controlled trial of transurethral microwave thermotherapy. Br J Urol 79(3):389-93.

Netto NR Jr, De Lima ML, Lucena R, Lavoura NS, Cortado PL, Netto MR. Is transurethral vaporization a remake of transurethral resection of the prostate. J Endourol 1999 Oct;13(8):591-4.

Nielsen HO. Transurethral prostatotomy versus tranurethral prostatectomy in benign prostatic hypertrophy. A prospective randomized study. Br J Urol 1988;61:435-8.

Noble SM, Coast J, Brookes S, Neal DE, Abrams P, Peters TJ, Donovan JL. Transurethral prostate resection, noncontact laser therapy or conservative management in men with symptoms of benign prostatic enlargement? An economic evaluation. J Urol 2002 Dec 01;168(6):2476-82.

Norby B, Nielsen HV, Frimodt-Moller PC. Transurethral interstitial laser coagulation of the prostate and transurethral microwave thermotherapy vs transurethral resection or incision of the prostate: results of a randomized, controlled study in patients with symptomatic benign prostatic [tr. BJU Int 2002 Dec;90(9):853-62.

Norlen H, Dimberg M, Allgen LG, Vinnars E. Water and electrolytes in muscle tissue and free amino acids in muscle and plasma in connection with transurethral resection of the prostate. II. Isotonic 2.2% glycine solution as an irrigating fluid. Scand J Urol Nephrol 1990;24(2):95-101.

Office of Science Coordination and Communication. Guidance for institutional review boards and clinical investigators. Drugs and biologics. [Internet]. Rockville (MD): U.S. Food and Drug Administration; 1998 Sep [cited 2003 Aug 19]. [11 p]. Available: http://www.fda.gov/oc/ohrt/irbs/drugsbiologics.html.

Ogden CW, Reddy P, Johnson H, Ramsay JW, Carter SS. Sham versus transurethral microwave thermotherapy in patients with symptoms of benign prostatic bladder outflow obstruction. Lancet 1993 Jan 2;341(8836):14-7.

Oh BR, Kim SJ, Moon JD, Kim HN, Kwon DD, Won YH, Ryu SB, Park YI. Association of benign prostatic hyperplasia with male pattern baldness. Urology 1998 May;51(5):744-8.

Olsson J, Nilsson A, Hahn RG. Symptoms of the transurethral resection syndrome using glycine as the irrigant. J Urol 1995 Jul;154(1):123-8.

O'Mallry AJ, Normand ST, Kuntz RE. Application of models for multivariate mixed outcomes to medical device trials: coronary artery stenting. Stat Med 2003 Jan;22(2):313-36.

Orandi A. Transurethral incision of prostate compared with transurethral resection of prostate in 132 matching cases. J Urol 1987 Oct;138(4):810-5.

Paterson RF, Lingeman JE. Holmium laser prostatectomy. Curr Urol Rep 2001 Aug;2(4):269-76.

Patrick DL, Deyo RA. Generic and disease-specific measures in assessing health status and quality of life. Med Care 1989 Mar;27(3 Suppl):S217-32.

Perlmutter AP, Muschter R. Interstitial laser prostatectomy. Mayo Clin Proc 1998 Sep;73(9):903-7.

Perlmutter AP, Verdi J, Watson GM. Prostatic heat treatments for urinary outflow obstruction. J Urol 1993 Nov;150(5 Pt 2):1603-6.

Perrin P. TUMT versus sham in BPH patients. In: Laduc R, Weil EH, Zerbib M, Perrin P, Denis L. Thermotherapy and hyperthermia workshop. Prog Clin Biol Res 1994;386:487-98.

Petas A, Isotalo T, Talja M, Tammela TL, Valimaa T, Tormala P. A randomised study to evaluate the efficacy of a biodegradable stent in the prevention of postoperative urinary retention after interstitial laser coagulation of the prostate. Scand J Urol Nephrol 2000 Aug;34(4):262-6.

Premarket approval (PMA) database for Prostatron system, hyperthermia. P950014. [internet]. Rockville (MD): U.S. Food and Drug Administration, Center for Devices and Radiological Health (CDRH); 1999 Nov 26 [cited 2003 Sep 02]. [1 p]. Available: http://www.accessdata.fda.gov.

Premarket approval (PMA) database for Urologix Targis (tm) system. P970008. [internet]. Rockville (MD): U.S. Food and Drug Administration, Center for Devices and Radiological Health (CDRH); 1999 Dec 16 [cited 2003 Sep 02]. [1 p]. Available: http://www.accessdata.fda.gov.

Proceedings of the fifth international consultation on BPH. Plymouth (UK): Health Publication Ltd.; 2001. 535 p.

Puppo P. Long-term effects on bph of medical and instrumental therapies. Eur Urol 2001 Mar;39 Suppl 6:2-6.

Pypno W, Husiatynski W. Treatment of a benign prostatic hyperplasia by Nd:YAG laser - own experience. Eur Urol 2000 Aug;38(2):194-8.

Ramsey EW, Dahlstrand C. Durability of results obtained with transurethral microwave thermotherapy in the treatment of men with symptomatic benign prostatic hyperplasia. J Endourol 2000 Oct;14(8):671-5.

Revicki DA, Leidy NK, Howland L. Evaluating the psychometric characteristics of the Psychological General Well-Being Index with a new response scale. Qual Life Res 1996 Aug;5(4):419-25.

Riehmann M, Knes JM, Heisey D, Madsen PO, Bruskewitz RC. Transurethral resection versus incision of the prostate: a randomized, prospective study. Urology 1995 May;45(5):768-75.

Rivas DA, Bagley D, Gomella LG, Hirsch IH, Hubert C, Lombardo S, McGinnis DE, Mulholland SG, Shenot PJ, Strup SE, Vasavada SP. Transurethral microwave thermotherapy of the prostate without intravenous sedation: results of a single United States center using both low- and high-energy protocols. TJUH TUMT Study Group. Tech Urol 2000 Dec;6(4):282-7.

Roberts RO, Jacobsen SJ, Jacobson DJ, Rhodes T, Girman CJ, Lieber MM. Longitudinal changes in peak urinary flow rates in a community based cohort. J Urol 2000 Jan;163(1):107-13.

Roehrborn CG, Bartsch G, Kirby R, Andriole G, Boyle P, de la Rosette J, Perrin P, Ramsey E, Nordling J, De Campos Freire G, Arap S. Guidelines for the diagnosis and treatment of benign prostatic hyperplasia: a comparative, international overview. Urology 2001 Nov;58(5):642-50.

Roehrborn CG, Burkhard FC, Bruskewitz RC, Issa MM, Perez-Marrero R, Naslund MJ, Shumaker BP. The effects of transurethral needle ablation and resection of the prostate on pressure flow urodynamic parameters: analysis of the United States randomized study. J Urol 1999 Jul;162(1):92-7.

Roehrborn CG, McConnell JD, Barry MJ, Benaim EA, Blute ML, Bruskewitz R, Holtgrewe HL, Kaplan SA, Lange JL, Lowe FC, Roberts RG, Stein B. AUA guideline on the management of benign prostatic hyperplasia. American Urological Association Education and Research, Inc. 2003. Available: http://www.auanet.org/timssnet/products/guidelines/bph_management.cfm.

Roehrborn CG, Preminger G, Newhall P, Denstedt J, Razvi H, Chin LJ, Perlmutter A, Barzell W, Whitmore W, Fritzsch R, Sanders J, Sech S, Womack S. Microwave thermotherapy for benign prostatic hyperplasia with the Dornier Urowave: results of a randomized, double-blind, multicenter, sham-controlled trial. Urology 1998 Jan;51(1):19-28.

Roehrborn CG. The placebo effect in the treatment of benign prostatic hyperplasia. In: Kirby RS, McConnell JD, Fitzpatrick JM, Roehrborn CG, Boyle P, editors. Textbook of benign prostatic hyperplasia. Oxford (UK): Isis Medical Media; 1996.

Roos NP, Wennberg JE, Malenka DJ, Fisher ES, McPherson K, Andersen TF, Cohen MM, Ramsey E. Mortality and reoperation after open and transurethral resection of the prostate for benign prostatic hyperplasia. N Engl J Med 1989 Apr 27;320(17):1120-4.

Rothmann M, Li N, Chen G, Chi GY, Temple R, Tsoi HH. Design and analysis of non-inferiority mortality trials in oncology. Stat Med 2003 Jan;22(2):239-64.

Salinas Sanchez AS, Hernandez Millan IR, Segura Martin M, Lorenzo Romero JG, Virseda Rodriguez JA. The impact of benign prostatic hyperplasia surgery on patients' quality of life. Urol Int 2002;68(1):32-7.

Saporta L, Aridogan IA, Erlich N, Yachia D. Objective and subjective comparison of transurethral resection, transurethral incision and balloon dilatation of the prostate. A prospective study. Eur Urol 1996;29(4):439-45.

Sarma AV, Jacobsen SJ, Girman CJ, Jacobson DJ, Roberts RO, Rhodes T, Lieber M. Concomitant longitudinal changes in frequency of and bother from lower urinary tract symptoms in community dwelling men. J Urol 2002 Oct;168(4 Pt 1):1446-52.

Schatzl G, Madersbacher S, Djavan B, Lang T, Marberger M. Two-year results of transurethral resection of the prostate versus four 'less invasive' treatment options. Eur Urol 2000 Jun;37(6):695-701.

Schatzl G, Madersbacher S, Lang T, Marberger M. The early postoperative morbidity of transurethral resection of the prostate and of 4 minimally invasive treatment alternatives. J Urol 1997 Jul;158(1):105-10; 110-1.

Schelin S. Mediating transurethral microwave thermotherapy by intraprostatic and periprostatic injections of mepivacaine epinephrine: effects on treatment time, energy consumption, and patient comfort. J Endourol 2002 Mar;16(2):117-21.

Schulz MW, Chen J, Woo HH, Keech M, Watson ME, Davey PJ. A comparison of techniques for eliciting patient preferences in patients with benign prostatic hyperplasia. J Urol 2002 Jul;168(1):155-9.

Sech SM, Montoya JD, Bernier PA, Barnboym E, Brown S, Gregory A, Roehrborn CG. The so-called 'placebo effect' in benign prostatic hyperplasia treatment trials represents partially a conditional regression to the mean induced by censoring. Urology 1998;51:242-50.

Sengor F, Kose O, Yucebas E, Beysel M, Erdogan K, Narter F. A comparative study of laser ablation and transurethral electroresection for benign prostatic hyperplasia: results of a 6-month follow-up [published erratum appears in Br J Urol 1997 Feb;79(2):304]. Br J Urol 1996 Sep;78(3):398-400.

Shalev M, Richter S, Kessler O, Shpitz B, Fredman B, Nissenkorn I. Long-term incidence of acute myocardial infarction after open and transurethral resection of the prostate for benign prostatic hyperplasia. J Urol 1999 Feb;161(2):491-3.

Shingleton WB, Farabaugh P, May W. Three-year follow-up of laser prostatectomy versus transurethral resection of the prostate in men with benign prostatic hyperplasia. Urology 2002 Aug;60(2):305-8.

Shingleton WB, Kolski J, Renfroe DL, Fowler JE Jr. Electrovaporization of the prostate versus laser ablation of the prostate in men with benign prostatic hypertrophy: a pressure-flow analysis. Urol Int 1998 Aug;60(4):224-8.

Shingleton WB, Renfroe LD, Kolski JM, Fowler JE Jr. A randomized prospective study of transurethral electrovaporization vs laser ablation of the prostate in men with benign prostatic hypertrophy. Scand J Urol Nephrol 1998 Jul;32(4):266-9.

Shingleton WB, Terrell F, Renfroe DL, Kolski JM, Fowler JE Jr. A randomized prospective study of laser ablation of the prostate versus transurethral resection of the prostate in men with benign prostatic hyperplasia. Urology 1999 Dec;54(6):1017-21.

Shokeir AA, al-Sisi H, Farage YM, el-Maaboud MA, Saeed M, Mutabagani H. Transurethral prostatectomy: a prospective randomized study of conventional resection and electrovaporization in benign prostatic hyperplasia. Br J Urol 1997 Oct;80(4):570-4.

Simpson RJ, Fisher W, Lee AJ, Russell EB, Garraway M. Benign prostatic hyperplasia in an unselected community-based population: a survey of urinary symptoms, bothersomeness and prostatic enlargement. Br J Urol 1996 Feb;77(2):186-91.

Soonawalla PF, Pardanani DS. Transurethral incision versus transurethral resection of the prostate. A subjective and objective analysis. Br J Urol 1992 Aug;70(2):174-7.

Sox HC Jr, Blatt MA, Higgins MC, Marton KI. Medical decision making. Newton (MA): Butterworth-Heinemann; 1988. 406 p.

Stewart AL, Ware JE, Sherbourne DC, Wells KB. Psychological distress/well-being and cognitive functioning measures. In: Stewart AL, Ware JE, editors. Measuring functioning and well-being: the medical outcomes study approach. Durham (NC): Duke University Press; 1992. p. 102-42.

Stoevelaar HJ, McDonnell J. Changing therapeutic regimens in benign prostatic hyperplasia. Clinical and economic considerations. Pharmacoeconomics 2001;19(2):131-53.

Suvakovic N, Hindmarsh JR. A step towards day case prostatectomy. Br J Urol 1996 Feb;77(2):212-4.

Talic RF, El Tiraifi A, El Faqih SR, Hassan SH, Attassi RA, Abdel-Halim RE. Prospective randomized study of transurethral vaporization resection of the prostate using the thick loop and standard transurethral prostatectomy. Urology 2000 Jun;55(6):886-90; discussion 890-1.

Tan AH, Gilling PJ. Holmium laser prostatectomy: current techniques. Urology 2002 Jul;60(1):152-6.

te Slaa E, De Wildt MJ, Debruyne FM, De Graaf R, De La Rosette JJ. Urinary tract infections following laser prostatectomy: is there a need for antibiotic prophylaxis? Br J Urol 1996 Feb;77(2):228-32.

Teillac P. Relief of BPO or improvement in quality of life. Eur Urol 1998;34(Suppl 2):3-9.

Trachtenberg J, Roehrborn CG. Updated results of a randomized, double-blind, multicenter sham-controlled trial of microwave thermotherapy with the Dornier Urowave in patients with symptomatic benign prostatic hyperplasia. Urowave Investigators Group. World J Urol 1998;16(2):102-8.

Tucker RD, Sievert CE, Kramolowsky EV, Vennes JA, Silvis SE. The interaction between electrosurgical generators, endoscopic electrodes, and tissue. Gastrointest Endosc 1992 Mar-Apr;38(2):118-22.

Tuhkanen K, Heino A, Ala-Opas M. Contact laser prostatectomy compared to TURP in prostatic hyperplasia smaller than 40 ml Six-month follow-up with complex urodynamic assessment. Scand J Urol Nephrol 1999 Feb;33(1):31-4.

Tuhkanen K, Heino A, Alaopas M. Hybrid laser treatment compared with transurethral resection of the prostate for symptomatic bladder outlet obstruction caused by a large benign prostate: a prospective, randomized trial with a 6-month follow-up. BJU Int 1999 Nov;84(7):805-9.

Tuhkanen K, Heino A, Ala-Opas M. Two-year follow-up results of a prospective randomized trial comparing hybrid laser prostatectomy with TURP in the treatment of big benign prostates. Scand J Urol Nephrol 2001 Jun;35(3):200-4.

U.S. Food and Drug Administration, Center for Devices and Radiological Health. 510(k) summary of safety and effectiveness. SLT CL MD contact laser system and delivery fibers. K972548. Rockville (MD): U.S. Food and Drug Administration, Center for Devices and Radiological Health; 1998 Apr 28. 4 p. Also available: http://www.fda.gov.

Urologix. Prostatron treatment. [internet]. Minneapolis (MN): Urologix, Inc.; 2003 [cited 2003 Aug 12]. [1 p]. Available: http://www.urologix.com.

van Agt HM, Essink-Bot ML, Krabbe PF, Bonsel GJ. Test-retest reliability of health state valuations collected with the EuroQol questionnaire. Soc Sci Med 1994 Dec;39(11):1537-44.

Van Melick HH, Van Venrooij GE, Eckhardt MD, Boon TA. A randomized controlled trial comparing transurethral resection of the prostate, contact laser prostatectomy and electrovaporization in men with benign prostatic hyperplasia: urodynamic effects. J Urol 2002 Sep;168(3):1058-62.

van Swol CF, van Vliet RJ, Verdaasdonk RM, Boon TA. Electrovaporization as a treatment modality for transurethral resection of the prostate: influence of generator type. Urology 1999 Feb;53(2):317-21.

van Venrooij GE, Boon TA. The value of symptom score, quality of life score, maximal urinary flow rate, residual volume and prostate size for the diagnosis of obstructive benign prostatic hyperplasia: a urodynamic analysis. J Urol 1996 Jun;155(6):2014-8.

Venn SN, Montgomery BS, Sheppard SA, Hughes SW, Beard RC, Bultitiude MI, Lloyd-Davies RW, Tiptaft RC. Microwave hyperthermia in benign prostatic hypertrophy: a controlled clinical trial. Br J Urol 1995 Jul;76(1):73-6.

Vuorinen J. A practical approach for the assessment of bioequivalence under selected higher-order cross-over designs. Stat Med 1997 Oct 15;16(19):2229-43.

Wada S, Yoshimura R, Kyo M, Hase T, Masuda C, Watanabe Y, Ikemoto S, Kawashima H, Kishimoto T. Comparative study of transurethral laser prostatectomy versus transurethral electroresection for benign prostatic hyperplasia. Int J Urol 2000 Oct;7(10):373-7.

Wagrell L, Schelin S, Nordling J, Richthoff J, Magnusson B, Schain M, Larson T, Boyle E, Duelund J, Kroyer K, Ageheim H, Mattiasson A. Feedback microwave thermotherapy versus TURP for clinical BPH--a randomized controlled multicenter study. Urology 2002 Aug;60(2):292-9.

Wang SJ, Hung HM. TACT method for non-inferiority testing in active controlled trials. Stat Med 2003 Jan;22(2):227-38.

Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992 Jun;30(6):473-83.

Warwick RT. A urodynamic review of bladder outlet obstruction in the male and its clinical implications. Urol Clin North Am 1979 Feb;6(1):171-92.

Welch G, Weinger K, Barry MJ. Quality-of-life impact of lower urinary tract symptom severity: results from the Health Professionals Follow-up Study. Urology 2002 Feb;59(2):245-50.

Yachia D, Aridogan IA. Comparison between first-generation (fixed-caliber) and second-generation (self-expanding, large caliber) temporary prostatic stents. Urol Int 1996;57(3):165-9.

Yerushalmi A, Fishelovitz Y, Singer D, Reiner I, Arielly J, Abramovici Y, Catsenelson R, Levy E, Shani A. Localized deep microwave hyperthermia in the treatment of poor operative risk patients with benign prostatic hyperplasia. J Urol 1985 May;133(5):873-6.

Zeitlin SI. Heat therapy in the treatment of prostatitis. Urology 2002 Dec;60(6 Suppl):38-40.

Zlotta AR, Djavan B. Minimally invasive therapies for benign prostatic hyperplasia in the new millennium: long-term data. Curr Opin Urol 2002 Jan;12(1):7-14.

Zorn BH, Bauer JJ, Ruiz HE, Thrasher JB. Randomized trial of safety and efficacy of transurethral resection of the prostate using contact laser versus electrocautery. Tech Urol 1999 Dec;5(4):198-201.