ALBERTA HEALTH TECHNOLOGIES DECISION PROCESS

Photoselective vaporization of the prostate (PVP) for the treatment of benign prostatic hyperplasia (BPH)

Final Report

(submitted by Dev Menon, School of Public Health, University of Alberta, May 2007)

EXECUTIVE SUMMARY

Introduction: Photoselective vaporization of the prostate (PVP) for the treatment of benign prostatic hyperplasia (BPH) was introduced approximately 3 years ago in North America. Although the diffusion of the KTP laser, used for PVP, has been quite limited in Canada, there is growing interest among some urologists and provincial governments. In this report, we review the safety, efficacy and effectiveness of PVP compared to the existing "gold standard", transurethral resection of the prostate (TURP), and consider the potential social, fiscal and economic factors involved in providing PVP as a funded service.

Safety and efficacy: A comprehensive literature search (using bibliographic databases, the world wide web and manual techniques) was conducted to identify studies comparing PVP and TURP. Fourteen studies (2 comparative and 12 non-comparative) were selected for analysis. A total of 12 adverse events/complications were identified in this body of literature; the rates of these complications were similar in both PVP and TURP populations. In addition, none of the PVP patients required a blood transfusion, compared to the reported rates of 5% to 11% for TURP patients. Finally, PVP patients were shown to have a significantly lower likelihood of developing clot retention, compared to TURP patients. Collectively, the 14 studies lead to the conclusion that PVP appears to be a safe procedure.

A number of outcomes were examined to determine efficacy/effectiveness. PVP appeared to be favourable to TURP when length of hospitalization and catheterization times were compared (the difference is statistically significant). There were no differences between the two procedures regarding operation times and re-operation rates. Regarding the primary clinical outcomes of

peak flow rates, post residual volumes and quality of life scores, there were no significant differences between the patient groups. Also, sexual function and PSA value changes were similar between the PVP and TURP groups

Four economic evaluations of PVP and TURP have been published in the past 4 years, from Canada, Switzerland, Australia and the United States. The common conclusion was that PVP is less costly per case that TURP. Our analysis shows that the cost differences are due to the cost of disposables, capital equipment and the length of hospitalization. The limited data from Canada (from the Ontario government and through personal communications) indicate that the cost of PVP is approximately half of that of TURP

RESPONSES TO POLICY-RELEVANT QUESTIONS

What is the prevalence and incidence of BPH?

- BPH is considered to be the most common condition in aging men. (See Part I: Prevalence of BPH).
- Approximately 25% of men over the age of 50 years in Canada have BPH (based on telephone survey of 500 randomly sampled men across Canada). (See Part I: Prevalence of BPH)

Does the prevalence or incidence vary by recognizable population groups?

- Prevalence increases with age. It is estimated that 40% to 60% of men over 60 years have BPH. (See Part I: Prevalence of BPH)
- Prevalence does not vary with race, culture, socioeconomic status (income and education level) or geographic region. (See Part I: Prevalence of BPH)
- In addition to age, known risk factors include prostate size and family history. (See Part I: Prevalence of BPH)

Does treatment vary across population groups?

- Treatment varies according to symptom severity, ranging from non-invasive to invasive alternatives (watchful waiting, medical management (drugs) and surgery). (See Part I: Management of BPH)
- Surgical options may be limited for patients in high surgical risk groups (e.g., anti-coagulated patients). (See Part I: Management of BPH)

Does treatment significantly reduce the burden of illness?

For moderate/severe LUTS/BPH:

- Symptoms improve in approximately 70% of patients with medical management alone (assessed through symptom scores and quality of life scores and urinary flow measurements). (See Part I: Non-surgical approaches)
- Symptoms improve in approximately 90% of patients who receive TURP (assessed through symptom scores and quality of life scores and urinary flow measurements). Typically, medical management has failed in these patients. (See Part I: Surgical approaches)

What is the etiology for BPH?

- BPH is an overgrowth of the prostate gland (See Part I: Definition and description of BPH)
- As the prostate grows larger, it presses against the urethra and bladder, interfering with

normal urine flow. This leads to symptoms of urinary hesitancy, frequent urination, urinary tract infection, and urinary retention. (See Part I: Definition and description of BPH)

- The exact etiology of BPH is unclear; however, the condition is thought to be attributed to age-related hormonal changes. (See Part I: Definition and description of BPH)

What is the standard treatment algorithm for BPH?

- The main treatment strategies for BPH include watchful waiting, medical management (i.e., drug therapy), and surgery. (See Part I: Management of BPH)
- Canadian treatment guidelines for BPH recommend that therapy choices be governed by the severity of symptoms, bother, and patient preference. (See Part I: Management of BPH)
- Care patterns typically follow a continuum that begins with non-invasive alternatives and moves towards more invasive surgical interventions. (See Part I: Management of BPH)

What does PVP do differently compared to TURP or other minimally invasive procedures?

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- Unlike other laser therapies for BPH, PVP uses a unique KTP laser (PVP GreenLight®) that emits light at a wavelength of 532 nm, which is within the greenlight spectrum. This wavelength is strongly absorbed by hemoglobin, but not by water. (See Part I: Minimally invasive techniques)
- When applied to vascularized tissue, the laser light is instantly absorbed by the blood, quickly vaporizing and removing the tissue. (See Part I: Minimally invasive techniques)

What is the available evidence respecting safety?

- Based on findings from 14 studies, PVP has a similar safety profile to that of the current gold standard (TURP). (See Part II: Results – Safety)
- Complication/adverse event rates were similar and, in some cases lower than those associated with TURP. (See Part II: Results – Safety)
- The learning curve for PVP appears to be relatively short (approx. 5 procedures for urologists who have performed TURP). (See Part II: Results – Safety)

What are the *expected* benefits of PVP, what are the risks, and do the benefits outweigh the potential risks?

Expected benefits

• The expected benefits of PVP include shorter recovery times, reduced length of hospitalization, similar or fewer complications/adverse events, and similar or greater improvement in functional outcomes, when compared with TURP. (See Part II: Methods)

Risks

• The anticipated risks associated with PVP are similar to those with TURP. (See Part II: Methods)

Do expected benefits outweigh the risks?

• Yes (Part II: Methods)

What is the available evidence of benefit or effectiveness and what outcome measures are used?

Measurable outcomes of PVP include:

• Adverse events/complications

• Improved voiding ability (i.e., increased peak urinary flow (Qmax) and decreased post residual volume (PVR))

• Improved symptom scores (i.e., decreased AUA-SI or IPPS score)

• Improved quality of life score (i.e., decreased IPPS QoL score)

(See Part II: Methods)

Available evidence of benefit includes:

• 14 studies: 2 comparative (1 RCT and 1 bi-centre cohort study) and 12 non-comparative (case series), involving 1376 patients with a maximum follow-up of 2 years

• Using levels of evidence/critical appraisal criteria to assess study quality, the quantity and quality of evidence found are considered to be fair.

(See Part II: Results)

Does PVP reduce related or follow-up treatments or care activities?

• Within the first 2 years, follow-up treatment appears to be similar to that of TURP.

(See Part II: Results)

• Since studies have not been able follow patients for more than 2 years (the Greenlight PVP system became commercially available about 2.5 years ago), the long-term durability of PVP (i.e., need for re-treatment) is unknown. (See Part II: Results)

What follow-up care is required to maintain the outcomes?

• Length of catheterization, length of hospitalization, and need for blood transfusions are less for PVP than for TURP. (See Part II: Results)

• Follow-up care within 2 years appears to be similar to TURP. (See Part II: Results)

• Follow-up care after 2 years (i.e., need for re-treatment) is unknown. (See Part II: Results)

Do the outcomes depend on characteristics of patients or patient groups?

• Outcomes among high risk patients (such as those on anticoagulants, with large prostates, or who have a history of cardiovascular or cerebrovascular disease, MI, etc.) are similar to those in non-high risk patients (based on findings from 2 of the studies which included high risk patients). (See Part II: Results)

• Operating or lasing time was found to increase with prostate size. (See Part II: Results)

Do the outcomes depend on the training or experience of the provider?

• The learning curve with PVP appears to be short (no more than 5 procedures) (based on the results of an RCT where none of the physicians had performed more than 5 laser prostatectomies prior to the trial and rates of adverse events/ complications did not vary with physician experience). (See Part II: Results)

For what conditions has PVP been approved in Canada?

• In Canada, the Greenlight® PVP system has only been approved for the treatment of BPH (i.e., not prostate cancer) (Medical Devices Licensing Branch, Health Canada). (See Part I: Status of PVP in Canada)

• The higher powered Greenlight® HP system is currently under review by Health Canada for market approval). (See Part I: Status of PVP in Canada)

Is PVP considered an acceptable part of professional practice?

• The 2 hospitals that introduced PVP into Ontario have now incorporated it into everyday practice, performing the procedure on the majority of patients whom they treat (personal communication, Dr. Woods). (See Part I: Status of PVP Canada)

Are there any treatments that may be approved in the near future that might affect the utilization of PVP?

- The 120 Watt GreenLight® HPS or High Performance System is expected to receive approval from Health Canada this month. This high-powered system is designed to vaporize prostatic tissue with greater speed and flexibility, allowing for not only effective, but also efficient treatment of all gland sizes. Laboratory testing and early clinical experiences have demonstrated that the GreenLight HPS removes tissue roughly 75% to 125% more quickly than the current 80 Watt GreenLight® PV system. (See Part I: Status of PVP Canada)

Do the benefits of PVP out-weigh its costs?

- The estimated cost of TURP over 5 years in patients who received the procedure in Alberta between April 1, 1999, and March 31, 2000, $4 million (in 1999/2000 dollars, calculated from administrative health data using records of 1006 BPH (not prostate cancer) patients who received TURP in 1999-2000 – inpatient and outpatient visits were manually reviewed to identify relevant visits, with assistance from a medical transcriptionist and a urologist) (See Appendix I).
- Approximately $500,000 of the $4 million was spent on the treatment of adverse events. (See Appendix I).

- If we assume that:
  1) 1400 patients are treated in 2007-2008 (based on the fact that the number of patients climbed by 200 over a 5 year period from 1999-2000 to 2004-2005)
  2) The cost of treating adverse events within 5 years of follow-up is the same for PVP and TURP
  3) The current cost of a TURP procedure is approx. $3,437.87 (based hospital and physician fees) (from Alberta Health and Wellness costing report and schedule of medical benefits) and the expected cost of treating 1400 patients over the next 5 years is $889,000 ($700,000 x 1.27 inflation).

The total cost for treating that cohort would be $5.7 million.

• If we assume:

1) The cost of PVP (hospital and physician fee) will be the same in Alberta as is currently reported in Ontario (Note: Ontario figures for TURP are approximately the same as Alberta's).
2) Alberta purchases the new Greenlight® HP system, which functions in standard OR suites without the need for external water connections or specialized electrical utilities
3) An equipment amortization rate of 5% (approximately $72/procedure)
4) Maintenance costs of approximately $10,000 per year after the first year (which is covered in the warranty) (personal communication, D. Okamoto)

The 5 year cost of treating 1400 patients in 2007-2008 with PVP would be $2.69 million.

Therefore, the incremental difference of treating that single cohort is approximately $3.01 million. (See Part III. Economic and fiscal considerations)

PREAMBLE

Within the last 5 years, laser technologies have re-emerged as a promising alternative to transurethral resection of the prostate (TURP), the current 'gold standard' treatment for benign prostatic hyperplasia (BPH).[1] Such re-emergence has primarily been attributed to the development and introduction of a new laser technique called photoselective vaporization of the prostate (PVP).[2] This technique employs a high-powered potassium-titanyl-phosphate (KTP) laser (i.e., the GreenLight PVP, American Medical Systems, Minnetonka, MN) to vaporize the prostatic tissue, creating a prostate cavity with minimal blood loss, postoperative discomfort, and hospital stays.[3] Thus, awareness of the availability of PVP has generated significant interest among patients, providers, and payers, alike.

PURPOSE OF THE REPORT

The purpose of this report is to review the safety and effectiveness of PVP compared with TURP, as well as the social, fiscal, and economic considerations involved in providing it for the surgical treatment of BPH.

PART I: INTRODUCTION AND BACKGROUND

Definition and description of Benign Prostatic Hyperplasia (BPH)

Benign prostatic hyperplasia (BPH) is a chronic progressive condition that involves the non-cancerous proliferation of cells forming the prostate gland.[4,5] The prostate gland, comprising two lobes enclosed in a layer of tissue, surrounds the urethra, the canal through which urine passes out of the body. Therefore, as the cells proliferate and the prostate enlarges, the encapsulating tissue layer prevents it from expanding, causing the gland to press against or

squeeze the urethra and obstruct urinary flow. The bladder wall then becomes thicker and irritable, contracting when it contains only small amounts of urine. Eventually, the whole bladder weakens, and loses its ability to empty itself.[6-9] This narrowing of the urethra and partial emptying of the bladder create many of the lower urinary tract symptoms (LUTS) by which BPH is characterized clinically.[10] They include frequent urination, urgency, hesitancy or intermittency, nocturia (i.e., excessive urination at night), a sensation of incomplete emptying, weak urinary stream, and postvoid dribbling.[11] The extent to which symptoms are experienced by men with BPH varies. While they may be 'bothersome', primarily affecting quality of life and interfering with daily activities, they can worsen, leading to more serious health conditions, such as hematuria (i.e., blood in the urine), acute urinary retention (i.e., a sudden inability to urinate that requires catheterization), recurrent urinary tract infections, bladder stones, hydronephrosis (e.g., swelling of the kidneys), and renal insufficiency.[11-13] The exact etiology of BPH is unclear; however, the condition is thought to be attributed to age-related hormonal changes. [11]

Prevalence of BPH

BPH is considered the most common cause of LUTS among ageing men.[5] According to the results of several recently published, large population based studies in the United States (US), prevalence increases with age.[12,14-17] Of men surveyed, approximately 25% under 60 years of age and 40-60% over 60 years of age reported moderate-to-severe LUTS (also referred to as clinical BPH). [14-17] Across all studies, symptom severity was measured in a similar way, using the American Urological Association Symptom Index (AUA-SI). Internationally recognized and

widely adopted, this self-administered questionnaire has been shown to be a valid and reliable instrument for assessing the severity of symptoms associated with BPH.[12] Findings from the only comparable epidemiologic study conducted in Canada parallel those from the US.[18] Approximately 23% of 508 randomly sampled men over 50 years of age expressed experiencing moderate-to-severe LUTS. Also consistent with the US studies, prevalence was found to increase with age. Similar trends have been observed in Europe as well. Based upon the results of the largest observational study conducted to date, the TRIUMPH Study (TransEuropean Research into the Use of Management Policies for LUTS suggestive of BPH in Primary Healthcare), which examined the management of LUTS in 'real-life practice' across 6 European countries (France, Germany, Italy, Poland, Spain, and the United Kingdom), the prevalence of moderate-to-severe LUTS among European males over 50 years of age is approximately 25%.[19] Thus, given growing ageing populations in both Europe and North America and the chronic nature of the disease, such studies, collectively, highlight the importance of BPH as an ongoing significant health concern and source of healthcare expenditures.[20]

Urinary retention, which represents the final stage of progressive BPH, has been shown, through these same studies, to occur at an incidence of 3.1 to 6.8 episodes per 1000 person years.[21,22] Like those for moderate-to-severe LUTS, rates increase with age.[21-27] In comparison, the incidence of moderate-to-severe LUTS attributable to BPH has been reported to be approximately 15 episodes per 1000 person years.[19]

Risk factors for BPH

To date, 3 risk factors for clinical BPH have been identified: age, family history, and prostate size. Longitudinal, population-based studies from Europe and the United States, exploring the relationship between prevalence and a number of demographic and socioeconomic factors, have demonstrated that values do not vary with race, level of education, income, or region of residence (urban versus rural).[13,28] At present, no similar Canadian studies appear to be available.

Burden of BPH

Studies assessing the economic burden (i.e., the direct, indirect, and intangible costs) of BPH in Canada with Canadian data do not appear to be available. However, 3 recently published papers from the US may be used to provide rough estimates, recognizing that US health care administrative costs have been shown to be higher than those in Canada.[13,29-31] Based on analyses of Medicare data (to capture patients 65 years of age and older) and medical claims from beneficiaries in more than 25 different employer-sponsored health insurance plans across the country (to capture patients under 65 years of age), the annual per-person direct cost of managing BPH in the year 2000 was calculated to be approximately $3,000 Cdn, after adjusting for differences in insurance coverage, patient demographics, and health status.[13] To determine the indirect costs (e.g., lost hours from work for treatment), enrollment files, health care claims, and absence data from a subset of private employers were assessed. Overall, employees with the condition each missed about 1 day of work annually related to BPH, and 10% reported some

work loss due to health care encounters for BPH.[30] With respect to intangible costs, no studies attempting to examine pain and suffering associated BPH could be found.

Diagnosis of BPH

Clinical BPH is typically diagnosed on the basis of 3 characteristics: bladder outflow obstruction (BOO), lower urinary tract symptoms, and prostate enlargement.[32] Because different combinations of these characteristics can give rise to a range of clinical presentations, several evidence-based practice guidelines for the assessment of BPH have been developed and published by leading professional associations in the field over the past 5 years, including the American Urological Association (AUA) and the European Association of Urology (EAU).[33-35] In 2005, a Canadian set of guidelines, designed to reflect the social priorities, economics, manpower issues, medicolegal considerations, and practice trends in Canada's health care system, were released.[36] These guidelines, which have been implemented in many of the health regions across the country, contain a series of diagnostic tests grouped into 4 categories: mandatory, recommended, optional, and not recommended (Table 1).[36]

Table 1. Suggested use of diagnostic tests for assessing BPH according to the Canadian Diagnostic Guidelines

Level of use	Diagnostic test
Mandatory	• Medical history • Physical examination including digital rectal examination • Urinalysis
Recommended	• Formal symptom inventory • Prostate-specific antigen (PSA)
Optional	• Creatinine • Voiding diary • Uroflowmetry (i.e., uroflow) • Post-void residual measurement
Not recommended	• Cystoscopy • Cytology • Urodynamics • Radiological evaluation of the upper respiratory tract • Prostate ultrasound • Prostate biopsy

Regardless of guideline source, necessary tests consist of a comprehensive medical history, which includes a review of medications (prescription, over the counter, and herbal), a physical and digital rectal exam, and urinalysis (i.e., physical and chemical examination of the urine). Further, all of the guidelines recommend collecting a formal symptom inventory using a validated tool/instrument to provide an 'objective' assessment of symptom severity.[34-38] The AUA-SI (Appendix 2) mentioned above and the International Prostate Symptom Score (IPSS) (Appendix 2) comprise the 'gold standard' for measuring the severity of LUTS associated with BPH. These self-administered questionnaires are identical in terms of content and scoring systems, with one exception. The IPPS has incorporated an additional quality of life-related question (i.e., bother score) to summarize the overall impact of voiding symptoms.[34,35] Like its counterpart, it has undergone extensive validity and reliability testing, and has been deemed a clinically sensible and responsive tool.[39] Both the AUA-SI and IPSS are scored from 0 to 35, with higher values indicating greater symptom severity.[34,35] Unique to the Canadian guidelines is a recommendation for PSA testing in men 1) with at least a 10 year life expectancy, 2) whom knowledge of the presence of prostate cancer would change management of their condition, or 3) whose PSA measurement would change management of their voiding symptoms.[36] Among tests classified as 'optional', uroflowmetry, specifically peak or maximum urinary flow rate (Qmax) recorded in milliliters per second, is considered to be one of the most valuable non-invasive means of corroborating lower urinary tract obstruction.[40] Thus, it is frequently employed in clinical studies comparing outcomes of different treatment alternatives.[41,42] In addition to peak urinary flow, such studies often evaluate post-void residual volume (PVR).[34,36,41] PVR measures, through catheterization or ultrasound examination, the amount of urine remaining in the bladder after voiding.[41] Although an elevated PVR can indicate bladder dysfunction or a

neurogenic disorder (originating from the nervous system), as opposed to BPH, it remains a simple, accurate test for monitoring patients over time or pre- and post-treatment.[42] Lastly, serum creatinine levels may be obtained in order to assess renal function and exclude renal insufficiency from obstructive uropathy (where the flow of urine becomes blocked, backing up into the kidneys and injuring one or both of them). In men, the most common cause of obstructive uropathy is an enlarged prostate.[35]

Management of BPH

The goal of therapy for clinical BPH is two fold: 1) improved quality of life through effective relief of LUTS and reduced lifetime risk of adverse consequences of the disease (e.g., urinary retention).[43,44] To accomplish this, evidence-based clinical practice guidelines, which reflect patient preferences for less invasive options, diagnoses in primary care settings, and the slow progression of the disease, have been developed.[44] Treatments include watchful waiting, medical management (pharmaceuticals), and surgery (minimally invasive and conventional techniques), with care patterns following a continuum that begins with non-invasive alternatives (i.e., watchful waiting or pharmaceuticals) and moves towards more invasive surgical interventions as symptoms worsen over time.[44-46]

Non-surgical approaches

Watchful waiting, in which a physician monitors a patient's condition without intervention, is the most common approach in men with uncomplicated BPH.[40,47] For men with symptomatic BPH (AUA-SI or IPPS scores >7), first-line therapy consists of medical management using 2 different classes of drugs, alpha-blockers (α-blockers) and 5-alpha-reductase inhibitors.[13,34] Alpha

blockers relax the smooth muscles in the urinary tract by blocking the prostate's α_1-adrenoreceptors. This reduces tension within the bladder neck and prostate, increasing urinary flow.[43,47] Their main adverse effects include dizziness and orthostatic hypotension (i.e., low blood pressure when standing).[45] The second class of drugs, the 5-alpha-reductase inhibitors (5-ARIs), reduces levels of dihydrotestosterone, the hormone which promotes prostatic growth, causing the prostate to shrink in size.[45] Therefore, in contrast to the alpha-blockers, the 5-ARIs help to decrease the risk of disease progression. While sexual adverse effects (decreased libido and erectile difficulties) are often associated with 5-ARIs, they have been shown to be reversible and similar to watchful waiting after 1 year of treatment.[47]

Surgical approaches

In general, surgical interventions are considered 'last resort' options, reserved for patients with refractory urinary retention (i.e., not responded to treatment), acute urinary retention (i.e., sudden inability to initiate voiding), recurrent infection or moderate-to-severe LUTS/BPH where medical management has failed.[34-36]

Standard/conventional approaches

For decades, transurethral resection of the prostate (TURP) has comprised the reference or 'gold standard' treatment for the surgical management of BPH.[43] This endoscopic-guided procedure involves removal of the inner portion of the prostate by electrocautery. Specifically, a resectoscope containing a light, valves for controlling irrigating fluid, and an electrical loop for cutting tissue and sealing blood vessels is inserted into the urethra under general or spinal anesthesia. The scope's wire loop is then used to resect obstructing tissue, piece by piece, from

inside the gland, creating a hollow cavity. This resected tissue is carried into the bladder by irrigating fluid (sterile glycine) and periodically flushed out. At the end of the procedure, a urinary catheter is inserted into the bladder and continuous irrigation performed until the effluent is clear.[11] In general, patients with no complications are discharged the next day after passing a voiding trial. The most common short term complications of TURP include bleeding, clot retention (where large clots of blood become wedged in the urethra), urinary tract infection, and inability to void.[48] The significance of such complications depends, in part, on individual patient characteristics (e.g., the presence of co-morbidities managed with anticoagulation therapy).[11] An uncommon but potentially severe complication is TUR syndrome, caused by the absorption of irrigating fluid during the surgery and in the immediate postoperative period.[11,49] Symptoms, ranging from confusion, hypotension, bradycardia (resting heart rate of under 60 beats per minute), nausea, and vomiting to collapse, require immediate attention. Treatment usually involves saline infusions and diuretics. Long term complications of TURP include urethral stricture (narrowing of the urethra), bladder neck contracture (narrowing of the bladder outlet), recurrent hematuria (blood in the urine), retrograde ejaculation (failure of the bladder neck to close during ejaculation, allowing semen to be propelled into the bladder instead of out through the urethra), and impotence or erectile dysfunction (the inability to achieve or maintain an erection). Despite these complications, significant post-surgical improvements in symptoms have been observed in approximately 90% of TURP patients.[50] Moreover, several studies have demonstrated the long term durability of such outcomes over follow-up periods of 8 to 22 years.[51]

Based on an analysis of administrative data from Alberta Health and Wellness, approximately 1200 Albertans with BPH received TURP between April 1, 2004, and March 31, 2005.[52] This represented an increase of 200 procedures over the number performed during the 1999-2000 reporting year. For both years, the median length of hospital stay was 2 days. The total cost of treating the 1006 patients who received TURP in 1999-2000 (including procedural costs, the costs associated with the treatment of adverse events/complications and re-operation costs within a 5-year follow-up period) to Alberta Health and Wellness was approximately $3 million (Appendix 1). Roughly $434,000 of this was related to adverse events/complications.

Prior to the introduction of TURP, open prostatectomy comprised the 'best practice' approach for managing moderate to severe LUTS/BPH. This procedure involves removal of the inner portion of the prostate via perineal, retropubic, or suprapubic routes or laproscopically through a retropubic approach.[34,42] While through the years, numerous clinical studies reported fewer complications with open prostatectomy than with TURP, longer hospital stays and recovery periods have led to its limited use in current clinical practice.[51] Nevertheless, it has remained an option for patients with larger prostates (> 80 ml or cm^3) because of the increased risk of TUR syndrome that accompanies prolonged resection times.[34]

Over the years, surgical techniques that represent modified versions of standard TURP have been developed.[51] They include transurethral incision of the prostate (TUIP), transurethral vaporization of the prostate (TUVP) and transurethral vapor resection of the prostate (TUVRP). During TUIP, small cuts are made where the prostate meets the bladder, relaxing the opening to the bladder and decreasing resistance to the flow of urine. No prostatic tissue is removed.

Findings from several randomized controlled trials (RCTs) of TUIP versus TURP have suggested that, while TUIP may provide superior results in terms of complications such as bleeding and retrograde ejaculation, its efficacy at 2 years is comparable to TURP for only a subset of patients with smaller prostates (< 30 ml or cm^3).[53-59] Little evidence on the long term effectiveness of TUIP (beyond 2 years) appears to be available. TUVP is similar to TURP, but it uses a roller electrode to vaporize superficial layers of prostatic tissue while coagulating deeper layers.[60] Like TUIP, the results of several small trials have demonstrated that its primary benefit may be fewer bleeding complications.[60-62] The longest RCT (5 years) comparing TUVP to TURP involved patients with relatively small prostates (<35 ml), and reported similar relief from symptoms for the two procedures.[61] TUVRP, which evolved from TUVP, employs a thicker resection loop and increased electrosurgical settings to achieve the "hemostatic properties of TUVP with the efficacy of TURP".[63] Despite its introduction over 10 years ago, evidence from studies with follow-up periods beyond 1 year is limited.[63-67] Further, the results of available studies are conflicting, with some demonstrating no advantage over TURP and others reporting less bleeding and catheterization time with TUIP.

Minimally invasive techniques

While conventional TURP remains the gold standard, a number of alternative minimally invasive techniques have been developed over the last 15 years in an attempt to address its limitations. TURP is considered difficult to learn and complications have been shown to increase with prostate volume.[44] Further, with a growing ageing population, the need to: 1) control health care costs by managing BPH as a day case in an outpatient environment, 2) treat patients at high risk for surgery (such as those taking anticoagulant medications), and 3) manage large prostates with

ease has become increasingly clear. Such minimally invasive techniques commonly utilize microwave (transurethral microwave thermotherapy (TUMT)), radiofrequency (transurethral needle ablation (TUNA)), or different types of laser energy to heat prostatic tissue and induce coagulation.[11] In general, studies of TUMT have been limited by small numbers of participants, high drop-out rates during follow-up intervals, and variable findings.[68-71] With respect to TUNA, RCTs using TURP as the comparator found that, while the risk of adverse events was slightly lower in the TUNA group, overall improvement in symptoms after 5 years was superior in the TURP group.[72-75] Therefore, based on the evidence accumulated to date, neither TUMT nor TUNA appear likely to replace TURP.

Since its introduction over a decade ago, laser technology has evolved from coagulation to enucleation and vaporization.[1] Coagulative techniques involve the use of laser energy (usually from a neodymium:yttrium aluminum garnet (Ng:YAG) laser) to induce coagulative necrosis of the prostatic tissue. Such techniques include visual laser ablation of the prostate (VLAP) and interstitial laser coagulation (ILC). During VLAP, prostatic tissue is lased using a non-contact, side-firing technique to cause cogulative necrosis. The necrotic tissue is then gradually sloughed through the urethra, resulting in secondary ablation (removal) of the obstructive tissue.[76] In ILC, the laser is pushed directly into the prostatic tissue, emitting energy radially into such tissue. This creates intraprostatic lesions which, in turn, undergo reabsorption and secondary atrophy after a shrinking process that lasts several weeks.[77] In the case of both VLAP and ILC, long post-operative catheterization times, unpredictable outcomes, and high reoperation rates, observed through RCTs with TURP as the comparator, have restricted their use.[76-80] Enucleating techniques employ laser energy (from a Holmium (Ho):YAG laser) to cut the

prostatic lobes into small pieces that can be evacuated through a resectoscope sheath while dissecting the tissue down to the prostatic capsule.[81] Holmium laser enucleation of the prostate (HoLEP) has compared favorably with TURP in randomized studies.[81-86] While operating time was longer in the HoLEP group, perioperative morbidity was lower and catheterization time and hospital stays were shorter. Further, complication rates did not vary with prostate size.[86] Lastly, improvements in symptom scores and peak urinary flow rates were similar across groups. Despite such findings, a long learning curve associated with the technique has precluded its widespread acceptance.[1] Vaporization techniques involve the use of laser energy to vaporize prostatic tissue, resulting in the immediate creation of a prostate cavity with debulking of the gland.[2] This process requires significant thermal energy, and prior to the development of the potassium-titanyl-phosphate (KTP) laser, no technology appeared to be able to accomplish it efficiently.[44] The KTP laser (frequency-doubled Nd:YAG laser or greenlight laser) emits laser light at a wavelength of 532 nm, which is within the greenlight spectrum. This wavelength is strongly absorbed by hemoglobin, but not by water. Therefore, when applied to vascularized tissue, it becomes instantly absorbed by the blood, quickly vaporizing and removing affected tissue while leaving behind a very thin zone of coagulated tissue. This remaining zone is considered sufficient to reduce or even prevent post-operative bleeding, yet thin enough to minimize side effects and damage to surrounding tissue caused by significant coagulation. In the end, a relatively bloodless, TUR-like cavity is created.[1] This technique, known as photoselective vaporization of the prostate (PVP) because of its tissue-selective laser effects, has produced promising results in clinical studies of the first commercially available KTP laser system (i.e., 80 Watt KTP system or GreenLight PV).[3] Safety and efficacy data demonstrate the possibility of obtaining a large cavity with minimal bleeding and catheterization times. Further,

the technique appears to be relatively easy to master, with centres reporting short learning curves.[2] Therefore, given its potential to manage high and low surgical risk patients with any size of prostate as a day case, PVP has become regarded as the first technique to truly challenge TURP's position as the gold standard.

Status of PVP in Canada

Market status

The 80 Watt GreenLight PVP Surgical Laser System (angled delivery device and main unit) received market approval as a Class III device (moderate risk) from the Medical Devices Licensing Bureau of Health Canada in April 2003.[87] Thus, it has been commercially available in Canada for almost 3 years.

Diffusion of PVP

Introductory sites for PVP in Canada comprise 2 hospitals in Ontario. Over the past 2.5 years, these centres have performed approximately 300 procedures on prostates as large as 150 ml. The average length of stay was just under 7 hours, and most patients returned home with a catheter, which was subsequently removed within 24 hours postoperatively. Both sites have now begun using PVP for the majority of their TURP procedures.[88]

In November 2006, PVP was introduced into Alberta, with the purchase and installation of a GreenLight PVP system at the Queen Elizabeth II Hospital in Grand Prairie. However, to our knowledge, procedures using the system have not yet been performed.[89]

The absence of the GreenLight PVP in more hospitals across the country may be explained by the advent of the next generation system, the 120 Watt GreenLight HPS or High Performance System.[88] This high-powered system is designed to vaporize prostatic tissue with greater speed and flexibility, allowing for not only effective, but also efficient treatment of all gland sizes. Laboratory testing and early clinical experiences have demonstrated that the GreenLight HPS removes tissue roughly 75% to 125% more quickly than does its predecessor.[90] In late 2006, GreenLight HPS was approved for sale by the US Food and Drug Administration.[91] Currently, it is awaiting such approval from Health Canada. Once granted, the Greenlight HPS is expected to replace the GreenLight PVP in the market.[89]

Introduction of an advanced high performance PVP Laser system

With the support of the Ontario Ministry of Health, plans for the first multi-centered randomized controlled trial comparing the GreenLight HPS with TURP are already underway in Ontario.[88,89] Preliminary discussions around a potential role for Alberta in such a trial have also taken place with members of Alberta's urologic and health services research communities. More formal discussions are anticipated once market approval of the system has been received.[89]

PART II: SAFETY AND EFFICACY OF PVP

Methods of the Review

A systematic review of evidence from existing research on the safety and efficacy of PVP was performed using well-accepted, widely adopted, 'best-practice' review methods.[92,93]

1. Search for relevant studies

A search for any published or unpublished studies of PVP appearing in the international or national English language literature before December 2006 was completed. Prior to conducting the search, critical terms used to describe BPH and PVP, along with their likely synonyms (e.g., enlarged prostate, GreenLight PVP, etc.) were first identified by examining lists of controlled vocabulary terms (e.g., medical subject heading terms [MeSH]) used to index already known references in the medical literature. These terms were then combined to form a structured search strategy.

The search strategy was subsequently applied to several electronic bibliographic databases, covering biomedical, clinical, social science, and health services management-related topics, in order to identify relevant published literature (Table 2). Unpublished or non-peer-reviewed information (e.g., conference proceedings, technical papers, government-sponsored reports, clinical newsletters, editorials, commentaries, and promotional material from manufacturers) was located through internet searches using meta-browsers capable of scanning multiple file formats (e.g., PDF files). Key relevant web sites were also examined (Table 2).

For completeness, the electronic search was supplemented by a manual search of the most recent issues of major urological journals (listed in Table 2) and reference lists from relevant health

technology assessments, systematic reviews, and retrieved studies. Lastly, specialists involved in the surgical treatment of BPH were contacted in order to identify any unpublished pending or recently completed studies. They included the corresponding authors of identified studies, as well as local (i.e., within Canada) urologists who perform PVP and/or TURP . The manufacturer of the Greenlight PV Surgical Laser System was also contacted.

Table 2. Summary of search strategies applied to information sources

Source	Search Strategy (Number of records found)
Electronic bibliographic databases	
MEDLINE (1966 – September Week 2 2006)	1. exp Prostatic Hyperplasia/ (13593) 2. BPH.mp (4859) 3. benign.mp (104883) 4. prostat$.mp (97538) 5. hyperplas$.mp (76865) 6. 3 AND 4 AND 5 (9156) 7. OR/1-2 (14580) 8. OR/6-7 (15740) 9. PVP.mp (1994) 10. photoselective.mp (20) 11. vapor$.mp (16267) 12. vapour$.mp (4218) 13. OR/11-12 (20317) 14. KTP.mp (453) 15. potassium titanyl phosphate.mp (151) 16. greenlight.mp (8) 17. 9 or (10 and 13) (2002) 18. 14 or 15 or 16 (496) 19. 8 and (17 or 18) (51) **Total found: 51**
EMBASE (1988 – 2006 Week 33)	1. exp Prostatic Hyperplasia/ (10248) 2. BPH.mp (4189) 3. benign.mp (70878) 4. prostat$.mp (70478) 5. hyperplas$.mp (44084) 6. 3 AND 4 AND 5 (6269) 7. OR/1-2 (10907) 8. OR/6-7 (11545) 9. PVP.mp (1774) 10. photoselective.mp (25) 11. vapor$.mp (12805) 12. vapour$.mp (3117) 13. OR/11-12 (14763) 14. KTP.mp (457) 15. potassium titanyl phosphate.mp (177) 16. greenlight.mp (11) 17. 9 or (10 and 13) (1781) 18. 14 or 15 or 16 (519) 19. 8 and (17 or 18) (52)

	Total found: 52
Healthstar (1966 to August 2006)	1. exp Prostatic Hyperplasia/ (6724) 2. BPH.mp (2276) 3. benign.mp (49072) 4. prostat$.mp (46179) 5. hyperplas$.mp (23022) 6. 3 AND 4 AND 5 (4364) 7. OR/1-2 (6987) 8. OR/6-7 (7420) 9. PVP.mp (1164) 10. photoselective.mp (15) 11. vapor$.mp (11172) 12. vapour$.mp (1882) 13. OR/11-12 (12927) 14. KTP.mp (289) 15. potassium titanyl phosphate.mp (108) 16. greenlight.mp (5) 17. 9 or (10 and 13) (1168) 18. 14 or 15 or 16 (323) 19. 8 and (17 or 18) (39)
	Total found: 39
CINAHL (1982 to August Week 3 2006)	1. exp Prostatic Hyperplasia/ (541) 2. BPH.mp (171) 3. benign.mp (2391) 4. prostat$.mp (4506) 5. hyperplas$.mp (802) 6. 3 AND 4 AND 5 (232) 7. OR/1-2 (563) 8. OR/6-7 (585) 9. PVP.mp (22) 10. photoselective.mp (3) 11. vapor$.mp (1585) 12. vapour$.mp (50) 13. OR/11-12 (1631) 14. KTP.mp (9) 15. potassium titanyl phosphate.mp (3) 16. greenlight.mp (2) 17. 9 or (10 and 13) (25) 18. 14 or 15 or 16 (12) 19. 8 and (17 or 18) (5)
	Total found: 5
PsycINFO (1806 to August Week 4)	1. PVP.mp (29) 2. photoselective.mp (0) 3. vapor$.mp (386) 4. vapour$.mp (28) 5. OR/3-4 (403) 6. KTP.mp (2) 7. potassium titanyl phosphate.mp (0) 8. greenlight.mp (2) 9. 1 or (2 and 5) (29) 10. 6 or 7 or 8 (4)
	Total found: 4

AARP Ageline (1978 to August 2006)	1. exp Prostatic Hyperplasia/ (0) 2. BPH.mp (7) **Total found: 7**
All EBM Reviews – 3rd Quarter 2006 (Cochrane Database of Systematic Reviews; Database of Abstracts of Review of Effects; Cochrane Central Register of Controlled Trials; and ACP Journal Club	1. exp Prostatic Hyperplasia/ (777) 2. BPH.mp (481) 3. benign.mp (2421) 4. prostat$.mp (4309) 5. hyperplas$.mp (1855) 6. 3 AND 4 AND 5 (827) 7. OR/1-2 (904) 8. OR/6-7 (1027) 9. PVP.mp (107) 10. photoselective.mp (2) 11. vapor$.mp (1581) 12. vapour$.mp (115) 13. OR/11-12 (1673) 14. KTP.mp (38) 15. potassium titanyl phosphate.mp (13) 16. greenlight.mp (0) 17. 9 or (10 and 13) (107) 18. 14 or 15 or 16 (39) 19. 8 and (17 or 18) (7) **Total found: 7**
NASW Clinical Register (14th Edition)	1. exp Prostatic Hyperplasia/ (0) 2. BPH.mp (0) **Total found: 0**
PubMed (1951 – August 2006)	#1 (prostate* OR prostatic) AND hyperplasi* AND benign (9064) #2 KTP OR potassium titanyl phosphate OR potassium titanylphosphate (582) #3 ((photoselective OR photo-selective) AND vapo*) OR PVP (2155) #4 greenlight (10) #5 #1 AND (#2 OR #3 OR #4) (57) **Total found: 57**
Web of Science (1955 to August 20, 2006)	TS = (benign AND hyperplasia AND prostat* AND (vapo* OR PVP OR photoselective OR KTP)) *DocType = All document types; Language = All languages; Databases = SCI-EXPANDED,SSCI, A&HCI; Timespan 1900-2006* **Total found: 163**
ProQuest – Dissertations & Theses	(Benign prostatic hyperplasia OR BPH OR (hyperplasia AND prostate AND benign)) AND (photoselective vapo* OR KTP OR laser) **Total found: 6**
CRD - Health Technology Assessment Database / NHS Economic Evaluation Database (August 2006)	benign prostat* hyperplasia OR bph) AND laser **Total found: 4**
GPO Access (August 2006)	(Benign prostatic hyperplasia OR BPH) AND PVP **Total found: 13**
OCLC ArticleFirst	(kw: benign and kw: prostat* and kw: hyperplasia) and kw: laser

(August 2006)	**Total found: 97**
World wide web sites	
www.google.ca	Greenlight PV system; photoselective vaporization of the prostate; photoselective vaporisation of the prostate; photoselective vapourization of the prostate; photoselective vapourisation of the prostate; PVP; KTP laser
www.laserscope.com	Greenlight PV System
www.urologytimes.com	Greenlight PV system; photoselective vaporization of the prostate; photoselective vaporisation of the prostate; photoselective vapourization of the prostate; photoselective vapourisation of the prostate; PVP; KTP laser
www.auanet.org	benign prostatic hyperplasia OR BPH
www.urologyhealth.	(benign prostatic hyperplasia OR BPH) AND laser
www.fda.org	Greenlight PV System
www.hc-sc.gc.ca/ (Therapeutic Products Directorate Medical Devices Bureau)	Laserscope Greenlight PV Surgical Laser System
Manual searches	
Recent issues of relevant journals	• British Journal of Urology • Current Opinion in Urology • European Urology • International Journal of Urology • Journal of Endourology • The Journal of Urology • Urology • World Journal of Urology
Relevant conference proceedings (2002 – 2006)	• American Society for Laser Medicine and Surgery Abstracts • American Urological Association Conference Abstracts • Annual Congress of the European Association of Urology Abstracts

2. Selection of relevant studies

Results of both the electronic and manual searches were imported into Reference Manager Version 11.0 (software program for managing and using bibliographic citations). After removing duplicate entries, compiled citations (titles and abstracts, where available) were reviewed for relevancy in 2 stages by 2 independent reviewers. First, the titles and abstracts (where available) were screened. Then, the full manuscripts of those deemed to be potentially relevant were retrieved and assessed using a pre-defined set of study inclusion criteria (Table 3).

If doubt over a study's relevancy still remained, further information was sought from the author. In cases where multiple citations from the same investigators appeared to report on the same patient population from a particular institution, all but the most recent one (determined by publication date and, when necessary, correspondence with the author) were excluded.

Any discrepancies between reviewers were resolved through discussion. No third party adjudication was required. The level of consensus between reviewers was assessed during both stages using kappa statistics. Kappa values for Stage 1 and Stage 2 were 0.79 and 0.88, respectively, indicating excellent agreement. [94]

Table 3. Criteria for including studies in the review

Parameter	Inclusion Criteria	Exclusion Criteria
Study design	• Randomized or controlled (e.g., pseudo-randomized of quasi-randomized) trials • Non-randomized clinical trials • Retrospective, prospective, or concurrent cohort studies • Case or clinical series	
Participants	• Patients diagnosed with moderate-severe LUTS attributable to BPH who require surgical intervention	• Diagnosis of prostate cancer
Interventions	• Photoselective Vaporization of the Prostate (PVP) with 80 Watt KTP laser (Greenlight PV system)	
Comparators	• Transurethral resection of the prostate (TURP) (not required)	
Outcomes	*Primary* • Increase in peak urinary flow rate (Qmax) • Decrease in postvoid residual volume (PVR) • Decrease (i.e., improvement) in IPPS or AUA score • Decrease (i.e., improvement) in IPPS Quality of Life (QoL) Score *Secondary* • Reduction in prostate volume *Operative* • Operating time • Length of hospital stay • Length of catheterization • Blood transfusion	

3. Synthesis and critical appraisal of selected studies

Information from studies was systematically extracted by two independent reviewers using a standard, pre-tested data abstraction form and set of decision rules. The form contained elements for assessing the purpose and methods (e.g., setting, number of patients, treatment protocol,

outcome measures, etc.) of each study and the validity of results presented (Table 4). When required, missing data were sought from the primary or corresponding author. Once again, consensus between reviewers on the information collected was assessed with kappa statistics; K= 1.0, indicating perfect agreement. Lastly, information was double-entered into RevMan, a software program for managing information for systematic reviews (Cochrane Collaboration).

The quality of each study was scrutinized by 2 independent reviewers using validated, published critical appraisal guidelines and levels of evidence scales (Appendix 3).[94] Discrepancies were, as before, resolved through consensus and a kappa score was calculated. Agreement between reviewers was found to be excellent (K= 0.79).

Table 4. Summary of elements comprising the data abstraction form

Parameter	Description of information collected
Study design	• Setting • method of randomization, allocation concealment, and blinding, where appropriate • Funding sources
Participants	• Number of patients recruited, randomized or assigned to treatment groups (i.e., PVP or TURP), and included in subsequent analyses • Number of patients censored (due to incomplete follow up or loss to follow up) • Maximum length of follow up • Patient inclusion and exclusion criteria, along with the distribution of patients by age, prostate size, co-morbidities, and severity of symptoms
Interventions	• Actual number of patients who underwent treatment in each group • Any protocol violations • Proportion of patients in each treatment group who completed treatment as planned • Information on any further therapy received
Outcomes	• Changes in peak urinary flow rate, post voiding residual volume, IPPS/AUA symptom score, IPPS Quality of Life Score, and prostate volume • Operating time, length of hospital stay, length of catheterization, and adverse events

4. Data analysis

Qualitative

Information collected from studies was summarized in tabular form to more easily identify trends or patterns in findings reported across studies.

Quantitative

Results from individual studies were combined through meta-analyses to generate summary estimates for each of the outcomes of interest. For dichotomous data (e.g., adverse events) pooled relative risks, together with 95% confidence intervals, were calculated. When continuous data were presented (e.g., peak urinary flow, post voiding residual volume, change in symptom scores, etc), mean differences and 95% confidence intervals were pooled and a weighted mean difference calculated. All statistical analyses were conducted in accordance with intention to treat principles (i.e., patients were analyzed in the groups to which they were originally allocated, regardless of whether or not they received the assigned treatment).

Prior to performing meta-analyses, effect sizes among studies were tested for heterogeneity using the chi-squared statistic for heterogeneity, set at a significance level of <0.1. Only data considered to be sufficiently homogeneous were pooled.

Results

Fifty-four discrete citations were initially identified through the literature search. Of them, 14 met the selection criteria and were, therefore, included in the review: 12 case series, 1 RCT, and 1 multi-centered cohort study, representing a total of 1376 PVP procedures (Figure 1).[95-108]

Overall description of included studies

A brief description of the 14 selected studies is presented in Table 5.1. A summary of excluded studies, along with rationale for their exclusion, is presented in Table 5.2.

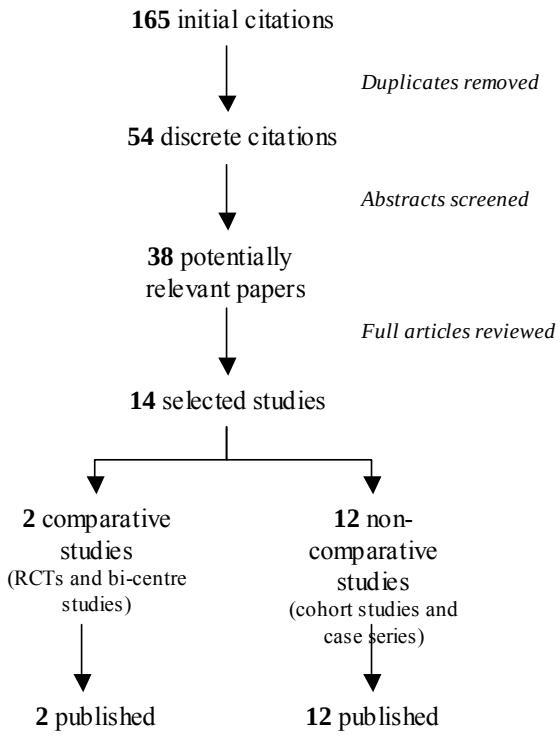

Figure 1. Results of literature search and study selection process

Across included studies, patients ranged from 44 years of age and 95 years of age, and had prostate sizes that varied from small (17 ml) to large (336 ml). The maximum length of time patients were followed after their procedure differed among studies. The majority used periods of either 6 months[95,101,103,105,106] or 12 months[96-99,100,104,107]. Only 1 monitored patients beyond 1 year, reporting outcomes at 24 months.[108] These follow-up periods reflect the short length of time for which the GreenLight PV system (the technology used to perform PVP) has been available to date (approximately 3 years). All but 1 of the studies assessed the safety of PVP, reporting adverse events/complications that occurred intra-operatively or within the early post-operative period. With respect to efficacy, a common set of primary outcome measures was

employed across all of the studies: namely maximum or peak urinary flow rate (Qmax), postvoid residual volume (PVR), and IPPS/AUA-SI symptom score. However, the types of secondary and operative outcomes measured varied.

Overall quality of included studies

The combined quality of the studies and, in turn, the strength of evidence presented was considered to be fair. Importantly, critical appraisal guidelines and levels of evidence scales generally rank studies according to study design. Therefore, both comparative studies[95,96] received high grades (A[95] and B[96]), while all 12 of the non-comparative studies (case series)[97-108] were assigned a lower grade (C). Lastly, given the newness of PVP, the number of studies (i.e., the evidence) is limited.

Safety

The following adverse events/complications were assessed: acute renal failure, urinary retention, clot retention, hematuria, dysuria, urinary tract infection, incontinence, urethral stricture, bladder neck contracture, bladder stenosis, and sexual dysfunction (Table 5.3). Based on pooled rates from the 12 case series, complication rates ranged from 0.0% for bladder stenosis to 9.3% for mild to moderate dysuria. When compared with those commonly reported for TURP[34], these values were either similar or considerably lower (urinary retention and clot retention). Further, none of the patients across the series required blood transfusions. In contrast, published transfusion rates for TURP range from 5% to 11%.[34] Similar trends were observed from pooled

analyses of relative risks (i.e., the ratio of the risk of an adverse event among patients receiving PVP to the risk among patients receiving TURP) for the 2 comparative studies (Table 5.4). With one exception (clot retention), none of the estimates were statistically significant, suggesting that, in general, the risk of experiencing a complication was comparable between treatment groups. Regarding clot retention, patients receiving PVP were shown to be significantly less likely to develop the condition. Importantly, the absolute values of estimates were interpreted conservatively, as both studies involved relatively small numbers of patients. Nonetheless, viewing the findings from all 14 studies collectively, PVP appears to be a safe procedure, carrying with it a risk of adverse events/complications that at worst, appears to be similar to the 'gold standard' treatment.

Lastly, the effect of physician experience on the risk of complications/adverse events was examined in one study to assess the learning curve associated with PVP.[96] Prior to study onset, physicians had each performed less than 5 laser prostatectomies. The results demonstrated no difference in complication rates as the number of procedures increased, suggesting that the procedure is relatively easy to master.

Efficacy

Operative outcomes

Operative outcomes assessed included operating time, length of hospital stay, duration of catheterization, and re-operation. Over the 12 case series, the average operating time ranged from 20 minutes to 137 minutes, and increased with preoperative prostate volume (i.e., longer

operating times were reported by studies involving larger prostates) (Table 5.5). Average catheterization times varied from 7.6 hours to 43 hours, and in 5 of the studies, a significant proportion of patients required no postoperative catheterization. In all but 1 of the studies, average hospital stays were less than 24 hours, with some patients going home in as little as 5 hours. Across studies that followed patients for 12 months, re-operation rates ranged from 0% to 7.5%. When values were compared with those published for TURP, PVP appeared favorable in terms of catheterization time and length of hospitalization.[34,49] Re-operation rates were similar for both procedures. These findings paralleled those from analyses of the 2 comparative studies (Table 5.6). No statistically significant differences in operating times and re-operation rates were observed between treatment groups. However, catheterization times and hospital stays were statistically significantly shorter for the PVP group.

Primary outcomes

Functional outcomes assessed included improvements in peak urinary flow (Qmax), peak residual volume (PVR), and symptom scores (IPPS or AUA-SI) from pre-operative or baseline values and were typically measured in 3 month intervals during the follow-up period. Despite variations in length of follow-up and timing of the first post-operative visit, all 12 case series reported comparable patterns of improvement in functional outcomes. Specifically, percent cumulative improvements in peak urinary flow rates, peak residual volumes, and symptom scores from pre-operative levels remained statistically significant throughout the follow-up period of each study (Tables 5.7, 5.8, and 5.9). Six of the series also measured changes in quality of life (bother) scores, reporting consistent statistically significant improvements over

time (Table 5.10). Lastly, pooled values were compared with those published for TURP at each follow-up point, and found to be similar (Tables 5.7 through 5.10). A meta-analysis of results from the first follow-up visit (i.e., the only data available for both studies) in the comparative studies demonstrated the same findings. There were no statistically significant differences in improvements in peak flow rates, post residual volumes, symptom scores or quality of life scores between treatment groups (Table 5.11).

Secondary Outcomes

Secondary outcomes assessed included sexual function and decreases in prostate-specific antigen (PSA) and prostate volume. Three of the 12 case series examined the effect of PVP on sexual functioning through a comparison of pre-and post procedural rates of erectile dysfunction.[100,101,102] No differences were found across studies. Only one of the comparative studies evaluated sexual function, with patients completing a self-administered questionnaire both prior to surgery and during each follow-up visit. No differences from baseline (i.e., pre-surgery) nor between the TURP and PVP groups were noted. PSA levels, measured in 4 of the case series and one of the comparative studies, decreased by approximately 30% to 40%, an amount similar to that reported for TURP. [95,97,99,105,107] Across the 5 case series and both comparative studies that assessed changes in prostate volume, 30% to 42% reductions were found. According to the results of the 2 comparative studies, these values were roughly equivalent to those for TURP.[95,96]

Performance of PVP in high risk groups

Two of the case series included patients on anticoagulants, among whom the prevalence of cardiovascular disease, cerebrovascular disease, and peripheral vascular disease was high (30%).[99,108] In all patients, PVP was performed successfully, with no reports of thromboembolic or bleeding events. No transfusions were required. Functional outcomes were similar to those reported for the non-high risk patients, suggesting that PVP may be both a safe and efficacious option for high-risk patients.

Durability of PVP

While the short-term efficacy of PVP appears similar to that of TURP, the lack of data beyond 2 years precludes assessment of its durability (i.e., long term efficacy).

PART III: ECONOMIC AND FISCAL CONSIDERATIONS

Methods

Review of existing economic analyses

1. Search for relevant economic analyses

Using an approach similar to that employed in the review of clinical studies, a comprehensive electronic and manual search for economic analyses comparing TURP with PVP was performed. This involved the information sources listed in Table 2, as well as EconLit (a bibliographic database of economics literature).

2. Selection and critical appraisal of relevant studies

All studies comparing the costs of TURP with those of PVP were included in the review. The quality of each study was assessed by two independent reviewers using published critical appraisal guidelines for economic evaluations.[109]

3. Analysis of information from included studies

Given the nature of included studies, analyses were limited to a narrative review of key findings.

Development of economic model comparing TURP with PVP in the Alberta

Based on findings from the review of clinical evidence for PVP compared with TURP, which demonstrated similar safety and efficacy profiles for the 2 treatments, a cost-minimization analysis was performed. Information on direct and indirect medical costs for TURP and PVP was collected from published literature, Alberta Health and Wellness (for TURP), the manufacturer (for PVP), and hospitals in Ontario where PVP is currently being performed.

Results

Summary of published economic analyses

Four studies describing costs associated with PVP were found: 2 peer-reviewed studies[110, 96], 1 conference abstract[111], and 1 government report[112].

Stovsky et al presented a Markov model (i.e., a type of model in which the progress of a disease with and without interventions is modeled in a sequence of time periods) comparing 5 types of

treatment for BPH, including PVP and TURP.[110] The analysis was performed from a U.S. Medicare Program perspective. Differences in outcomes between treatments were determined from published literature, including the American Urological Association BPH guidelines data set. The model followed patients for 2 years. All ICD-9-CM codes with a procedure for BPH were identified and included in the analysis. Direct medical costs in 2005 (cost of 7 adverse events, re-treatment, and follow-up care, including physician and hospital costs) were obtained from Medicare claims. No indirect costs were included. Total direct medical costs were calculated at 6 months, 12 months and 24 months. Sensitivity analyses were performed (a) on adverse event rates, (b) to determine the PVP re-treatment rate at which PVP and TURP costs become equal, and (c) by changing the Medicare claims rates from 2005 to 2006 figures. No discounting was performed, and no incremental cost-effectiveness parameters were calculated. The authors concluded that the estimated PVP costs are less than TURP cost during the 2 year period: per patient costs ranged from $3,020 US (at 6 months) to ($3,589 US) at 24 months for PVP compared to corresponding figures of $4,030 US and $4,754 US for TURP. Importantly, this study met most of the critical appraisal criteria applied to assess study quality.

Bouchier-Hayes conducted an economic evaluation alongside the single randomized controlled trial of PVP vs. TURP.[95] However, little information beyond a brief description of the cost per case for each treatment was presented. For patients who underwent TURP, the average cost per case was statistically significantly higher than for those who underwent PVP (TURP: AU$4,291.68; PVP: AU$3368.12) for those who received PVP. Because of the lack of information on sources of cost data, cost elements, performance of sensitivity analyses, and discounting, the quality of this study was considered to be poor.

Ruszat et al conducted on a prospective study of PVP (77 patients) versus TURP (28 patients).[111] Cost items included: surgical procedure, operating room costs, ward costs, physician fees and disposable and non-disposable materials. While costs for disposables (including laser fibres for PVP) were significantly higher for PVP, OR costs, hospitalization costs, and costs of post-operative nursing, as well as overall costs, were lower for PVP than for TURP. The limitations of this study were similar to those of Bouchier-Hayes, as much of the required details around costs were not reported.

The final study comprised a cost analysis of several treatments for BPH, including PVP and TURP, prepared by the Medical Advisory Secretariat of the Ontario Ministry of Health and Long-Term Care.[112] Categories of costs examined were: physician fees (surgeons, anesthetists and anesthetist assistants), hospital costs, operating time and blood transfusion costs. Sources of physician and hospital costs were government data sets, while operating time and blood transfusion costs were extracted from published literature. Capital costs were reported, but not incorporated in the calculations. The total cost per procedure was calculated, along with the impact on provincial expenditures for various possible rates of "diffusion" or utilization of the technologies. The authors concluded that the cost of PVP per procedure was the lowest ($1,184) while the corresponding figure for TURP was $3,887. Consequently, the impact on the government's budget of replacing TURP with PVP was found to be positive. Importantly, this analysis did not consider factors such as the cost of adverse events (such as urinary tract infection) and re-treatment costs..

Although the quality of the studied reviewed varied, the findings did not. All 4 demonstrated that, on a per-case or per-patient basis, PVP was cheaper than TURP.

Findings from the cost-minimization analysis

A list of relevant items for which costs may be estimated for PVP and TURP is provided in Table 5. The following assumptions were made:

1. The pre-operative physical examination by a physician and the diagnostic tests used to establish BPH are the same regardless of treatment choice. Thus, the pre-operative costs for both group are the same.

2. Physician and nurse costs for both groups are the same.

3. PVP requires the use of disposable laser fibres, which are estimated in the Ontario government report to each cost $650.[112] For TURP, a resecting loop is required; this has been estimated to cost $100 each. Regarding capital costs, TURP will already be available at the hospital or institution, so there will be no additional capital expenditures. PVP, as a new program, will require the purchase of a PVP GreenLight® laser system (specifically, the new, higher powered GreenLight® HPS), which is estimated to cost $125,000 (Personal communication, D. Okamoto, American Medical Systems, March 10, 2007). This system is built to function in standard OR suites without the need for external water connections or specialized electrical utilities. Therefore, it is assumed that no installation costs will be incurred. Maintenance costs after the first year (after the warranty has expired) are estimated to be $10,000 per year (Personal communication, D. Okamoto, American Medical Systems, March 10, 2007). The equipment is amortized over 5 years, with an average of 1400 procedures each year. However, early in its diffusion, the patient throughput will be considerably less, and so the annual amortized costs will be substantially greater.

4. PVP patients will require observation in a step-down day ward after their procedure. This will contribute to the costs of the PVP treatment. For the TURP patients, an average length of stay of 2 days is anticipated.[52]

5. There are no differences between the rates of complications/adverse events in the two groups. Also, based on the limited long-term data on PVP, it is assumed (conservatively) that the re-treatment rates will be the same in both groups.

Thus, it is clear that any difference in per treatment costs between PVP and TURP will be due to differences in costs of consumables, capital equipment and length of hospital stays. Even though there are sufficient data on these cost elements for TURP in Alberta, equivalent data for PVP does not exist. The only Canadian data is contained in the Ontario government report. This report estimates the cost of PVP per procedure to be less than half of that of TURP ($3,887 vs. $1,184). Even if the cost of capital depreciation and system maintenance are included (which the Ontario report does not do), the difference in cost will still be substantial. As the actual costs per TURP in Alberta is approximately $3,437.87 (based on Alberta Health costing data and physician fee schedules for 2005), it would not be unreasonable to expect PVP costs in Alberta to be between $1500 and $1800, which is still considerably cheaper than a TURP.

Table 5. Comparison of costs for TURP vs. PVP

Item	TURP ($ Cdn)	PVP ($ Cdn)	Data source
Pre-operative			
Physical examination	=	=	Alberta Health Care Insurance Plan Schedule of Medical Benefits – Medical Procedure List 2005 (SoMB)
Diagnostic tests (blood, urinalysis, etc)	=	=	Health costing in Alberta 2005 Annual Report
Operative			
Personnel			
• Circulating nurse	=	=	
• Scrub nurse	=	=	
• Urologist	=	=	Alberta SoMB
• Anaesthetist	=	=	Alberta SoMB

Consumables			
• Fiber	↓ (0)	↑ (650.0)	Ontario Health Technology Advisory Committee
• Loop	↑ (100)	↓ (0)	Personal communication (E. Woods)
• Capital (equipment)	↓ (0)	↑ (72.0*)	
Post-operative			
Days of hospitalization			
• Step-down unit	↓ (0)	↑ (?)	
• General inpatient ward/unit (2 days)	↑ (?)	↓ (0)	
Treatment of complications/adverse events)	=	=	Part II of this report
Post-discharge			
Treatment of complications/adverse events)	=	=	Part II of this report
Retreatment	=	=	

*$125,000 Cdn purchase price amortized over 7000 procedures in 5 years

PART 1V. SOCIAL CONSIDERATIONS

Methods

A comprehensive search for studies identifying any psycho-social implications of TURP, which may, in turn, be minimized through the use of PVP instead, was completed. Once again, the information sources identified in Table 3 were scanned, employing a search strategy that combined terms for TURP with those synonymous with psychosocial consequences (e.g., burden of illness or disease, social cost, psychological cost, personal cost, productivity loss; work loss, or quality of life). Since the purpose of the review was to highlight issues, the quality of studies was not appraised.

Results

No studies describing a 'burden' associated with TURP were found. In fact, several reporting high patient satisfaction rates (80%) as long as 10 years after TURP were located.[113] Further, the

findings of this report (Part II) suggest that improvements in quality of life and symptom scores are comparable for TURP and PVP, at least after 4 to 6 weeks of recovery. Nevertheless, none of the studies reviewed attempted to capture the 'value' of shorter hospital stays and catheterization times to patients. This may be significant, especially for patient who are employed.

Table 5.1 Summary of included studies

Study authors (year published)	Methods	Patients	Intervention	Outcomes	Study Quality*
Comparative studies					
Bachmann et al (2005)	Bi-centre cohort study - prospective - 2 hospitals in Switzerland (all TURPs performed at 1 centre and all PVPs performed at other centre) - recruitment at each centre: consecutive Country: Switzerland	Number of patients: 101 Mean age: 70.16 years Age range: not specified *Inclusion criteria* 1. Maximum urinary flow rate (Q_{max}) $\leq$ 15 mL/s OR postvoid residual volume > 100 mL 2. IPPS > 7 *Exclusion criteria* 1. Neurogenic bladder disorder 2. Urethral stricture 3. Postvoid residual volume > 400 mL 4. Acute or chronic urinary retention 5. Indwelling catheter	*PVP* Laser: 80 Watt KTP/532 nm laser (GreenLight PV™) Number of patients: 64 Mean age: 71 years Age range: not provided Surgeon experience: 4 surgeons, 2 experienced and 2 inexperienced *TURP* Standard technique (no special modifications) Number of patients: 37 Mean age: 71 years Age range: not provided Surgeon experience: 3 surgeons, each had performed >200 TURPs prior to study Note: No statistically significant differences between patient groups except in mean postvoid residual volume (PVP: 146.1 mL vs TURP: 120.7 mL)	*Primary outcomes* (Follow-up: discharge, 1 month, 3 months, and 6 months) 1. Maximum urinary flow rate 2. Postvoiding residual volume 3. IPPS score 4. IPPS Quality of Life (QoL) score *Secondary outcomes* (Follow-up: 1 month, 3 months, and 6 months) 1. Prostate volume 2. Prostate Specific Antigen (PSA) levels *Perioperative outcomes* 1. Operating time (minutes) 2. Length of hospital stay (hours) 3. Length of catheterization (hours) 4. Change in hemoglobin (mg/dL) *Adverse events/complications*	Grade: B Level of evidence: 2b
Bouchier-Hayes et al (2006)	Randomized Controlled Trial - protocol designed in accordance with American Urological Association guidelines - method of randomization not described - power assumptions not described - non-blinded - single centre - analyzed on intention to treat basis	Number of patients: 76 Mean age: 65.7 years Age range: 51 years to 81 years *Inclusion criteria* 1. Maximum urinary flow rate (Q_{max}) $\leq$ 15 mL/s 2. IPPS $\geq$ 12 3. Age > 50 years 4. Prostate volume 15-85 cm^3 5. Referred by family physician for LUTS 6. Obstructed bladder 7. Able to complete QoL,	*PVP* Laser: 80 Watt KTP/532 nm laser (GreenLight PV™) Number of patients: 38 Mean age: 65.2 years Age range: 51 years to 81 years *TURP* Standard technique (no special modifications) Number of patients: 38 Number of patients: 38 Mean age: 66.2 years Age range: 55 years to 80 years	*Primary outcomes* (Follow-up: 6 weeks, 3 month, 6 months, and 12 months) 1. Maximum urinary flow rate 2. Postvoiding residual volume 3. IPPS score 4. IPPS Quality of Life (QoL) score *Secondary outcomes* (Follow-up: 6 months) 1. Prostate volume *Perioperative outcomes* 1. Operating time (minutes) 2. Length of hospital stay (hours) 3. Length of catheterization (hours)	Grade: A Level of evidence: 1b

Study authors (year published)	Methods	Patients	Intervention	Outcomes	Study Quality*
	Country: Australia	symptom, and sexual function questionnaires *Exclusion criteria* 1. Neurogenic bladder disorder 2. Known or suspected prostate cancer 3. Postvoid residual volume > 400 mL 4. Chronic urinary retention 5. Taking finasteride or dutasteride	Surgeon experience (both trial arms): all surgeons had performed 35-325 TURPs and < 5 laser prostatectomies Note: No statistically significant differences in patients between treatment arms	4. Change in hemoglobin (mg/dL) *Adverse events/complications*	
Non-comparative studies					
Hai and Malek (2003)	Case series -prospective Country: United States	Number of patients: 10 Mean age: 64.1 years Age range: 58 years to 73 years *Inclusion criteria* 1. Candidate for TURP *Exclusion criteria* 1. Neurogenic bladder disorder 2. Prostate cancer 3. Urinary retention 4. Urethral stricture 5. Bladder neck contracture 6. Urinary tract infection	*PVP* Laser: 80 Watt KTP/532 nm laser (GreenLight PV™) Surgeon experience: not described	*Primary outcomes* (Follow-up: 1, 3, 6, and 12 months) 1. Maximum urinary flow rate 2. Postvoiding residual volume 3. AUA-SI score 4. AUA-QoL scores *Secondary outcomes* (Follow-up: 1, 3, 6, and 12 months) 1. Prostate Specific Antigen (PSA) levels 2. Prostate volume *Perioperative outcomes* 1. Operating time (minutes) 2. Length of catheterization (hours) *Adverse events/complications*	Grade: C Level of evidence: 4
Mattioli et al (2003) Abstract only	Case series - prospective Country: Italy	Number of patients: 65 Mean age: 65 years Age range: 48 years to 85 years *Inclusion criteria* - none specified	*PVP* Laser: 80 Watt KTP/532 nm laser (GreenLight PV™) Surgeon experience: not described	*Primary outcomes* (Follow-up: 12 months) 1. Maximum urinary flow rate 2. Postvoiding residual volume 3. AUA-SI score *Perioperative outcomes* 1. Operating time (minutes) 2. Length of catheterization (hours) 3. Length of hospital stay (hours)	Grade: C Level of evidence: 4
Sandhu et al (2004)	Case series - prospective Country: United States	Number of patients: 64 Mean age: 70.1 years Age range: 44 years to 92 years *Inclusion criteria* Patients with prostate volumes > 60 cm^3	*PVP* Laser: 80 Watt KTP/532 nm laser (GreenLight PV™) Surgeon experience: all procedures performed by same surgeon	*Primary outcomes* (Follow-up: 1, 3, 6, and 12 months) 1. Maximum urinary flow rate 2. Postvoiding residual volume 3. IPPS score *Secondary outcomes* (Follow-up: 6 or 12 months)	Grade: C Level of evidence: 4

Study authors (year published)	Methods	Patients	Intervention	Outcomes	Study Quality*
				1. Prostate Specific Antigen (PSA) levels *Perioperative outcomes* 1. Operating time (minutes) 2. Length of catheterization (hours) 3. Length of hospital stay (hours) *Adverse events/complications*	
Te et al (2004)	Multicentre study - prospective - 6 medical centres Country: United States	Number of patients: 139 Mean age: 67.7 years Age range: 45 years to 88 years *Inclusion criteria* 1. Maximum urinary flow rate (Q_{max}) $\leq$ 15 mL/s 2. postvoid residual volume $\leq$ 350 mL 3. AUA-SI > 12 4. Prostate volume >15-200 cm^3 *Exclusion criteria* 1. Neurogenic bladder disorder 2. Prostate cancer 3. PSA $\geq$ 10 ng/mL 4. Urethral stricture 5. Bladder neck contracture 6. Urinary incontinence 7. Prostatitis 8. Urinary tract infection 9. Serum creatinine $\geq$ 1.8 mg/dl	*PVP* Laser: 80 Watt KTP/532 nm laser (GreenLight PV™) Surgeon experience: not described	*Primary outcomes* (Follow-up: 1, 3, 6, and 12 months) 1. Maximum urinary flow rate 2. Postvoiding residual volume 3. AUA-SI score 4. AUA-QoL scores *Secondary outcomes* (Follow-up: 6 and 12 months) 1. Reduced prostate volume 2. Sexual function (also measured at 3 months) *Perioperative outcomes* 1. Operating time (minutes) 2. Length of catheterization (hours) 3. Length of hospital stay (hours) *Adverse events/complications*	Grade: C Level of evidence: 4
Barber et al Abstract only (2004)	Case series - prospective Country: United Kingdom	Number of patients: 30 Mean age: 66 years Age range: not provided *Inclusion criteria* - on routine waiting list for TURP	*PVP* Laser: 80 Watt KTP/532 nm laser (GreenLight PV™) Surgeon experience: not described	*Primary outcomes* (Follow-up: 6 months) 1. Maximum urinary flow rate 2. Postvoiding residual volume 3. IPSS score 4. IPPS QoL scores *Secondary outcomes* (Follow-up: 6 months) 1. Prostate volume 2. Erectile function (ITEF-5 Score) *Perioperative outcomes* 1. Length of catheterization (hours)	Grade: C Level of evidence: 4

Study authors (year published)	Methods	Patients	Intervention	Outcomes	Study Quality*
				3. Length of hospital stay (hours) *Adverse events/complications*	
Fu et al (2005)	Case series - prospective - multi-centre Country: China	Number of patients: 196 - refractory urinary retention: 58 - no refractory urinary retention: 138 Mean age: 75 years Age range: 50 years to 92 years *Inclusion criteria* - none specified - included patients with and without refractory urinary retention	*PVP* Laser: 80 Watt KTP/532 nm laser (GreenLight PV™) Surgeon experience: not described	*Primary outcomes* (Follow-up: 3 months) 1. Maximum urinary flow rate 2. Postvoiding residual volume 3. IPSS score 4. IPPS QoL scores *Secondary outcomes* 1. Sexual function *Perioperative outcomes* 1. Operating time (minutes) 2. Length of catheterization (hours) 3. Change in hemoglobin (g/dL) *Adverse events/complications*	Grade: C Level of evidence: 4
Park & Ha (2005) Abstract only	Case series - prospective - consecutive patients Country: South Korea	Number of patients: 82 Mean age: 82 years Age range: 51 years to 86 years *Inclusion criteria* - none specified	*PVP* Laser: 80 Watt KTP/532 nm laser (GreenLight PV™) -performed on out-patient basis Surgeon experience: not described	*Primary outcomes* (Follow-up: 6 months) 1. Maximum urinary flow rate 2. Postvoiding residual volume 3. IPPS score 4. IPPS Quality of Life (QoL) score *Perioperative outcomes* 1. Operating time (minutes) 2. Length of catheterization (hours) *Adverse events/complications*	Grade: C Level of evidence: 4
Sarica (2005)	Case series - prospective Country: Turkey	Number of patients: 240 Mean age: 67.4 years Age range: 46 years to 83 years *Exclusion criteria* 1. Urethral stricture 2. Neurogenic bladder 3. Urinary incontinence 4. Urinary tract infection 5. Compromised renal function	*PVP* Laser: 80 Watt KTP/532 nm laser (GreenLight PV™) Surgeon experience: not described	*Primary outcomes* (Follow-up: 6 and 12 months) 1. Maximum urinary flow rate 2. Postvoiding residual volume 3. IPSS score 4. IPPS QoL scores *Secondary outcomes* (Follow-up: 6 and 12 months) 1. Prostate volume *Perioperative outcomes* 1. Operating time (minutes) 2. Length of catheterization (hours) 3. Length of hospital stay (hours) *Adverse events/complications*	Grade: C Level of evidence: 4

Study authors (year published)	Methods	Patients	Intervention	Outcomes	Study Quality*
Volkan et al (2005)	Case series - prospective Country: Turkey	Number of patients: 186 Mean age: 66 years Age range: 47 years to 90 years *Inclusion criteria* 1. Maximum urinary flow rate (Q_{max}) < 10 mL/s 2. IPPS > 8 *Exclusion criteria* 1. Neurogenic bladder disorder 2. Prostate cancer 3. PSA > 4 ng/mL 4. Indwelling catheter 5. Urethral stricture 6. Previous prostate surgery 7. Prostate volume > 70 cm^3	*PVP* Laser: 80 Watt KTP/532 nm laser (GreenLight PV™) Surgeon experience: all procedures performed by 1 of 2 surgeons	*Primary outcomes* (Follow-up: 1, 3, and 6 months) 1. Maximum urinary flow rate 2. Postvoiding residual volume 3. IPPS score *Secondary outcomes* (Follow-up: 1 day, 15 days, 1 month, and 2 months) 1. Prostate Specific Antigen (PSA) levels *Perioperative outcomes* 1. Length of catheterization (hours) 2. Length of hospital stay (hours) 3. Change in hemoglobin (g/dL) *Adverse events/complications*	Grade: C Level of evidence: 4
Han et al Abstract only (2006)	Case series - prospective Country: South Korea	Number of patients: 104 Mean age: 66.1 years Age range: 51 years to 84 years *Inclusion criteria* 1. Maximum urinary flow rate (Q_{max}) ≤ 15 mL/s 2. AUA-SI ≥ 8 3. Age > 50 years *Exclusion criteria* 1. Neurogenic bladder disorder 2. Detrusor underactivity	*PVP* Laser: 80 Watt KTP/532 nm laser (GreenLight PV™) Surgeon experience: not described	*Primary outcomes* (Follow-up: 1, 3, and 6 months) 1. Maximum urinary flow rate 2. Postvoiding residual volume 3. AUA-SI score *Secondary outcomes* (Follow-up: 6 months) 1. Prostate volume *Perioperative outcomes* 1. Length of catheterization (hours) 3. Length of hospital stay (hours) *Adverse events/complications*	Grade: C Level of evidence: 4
Monoski et al (2006)	Case series - retrospective - consecutive patients Country: United States	Number of patients: 40 Mean age: not specified Age range: not specified *Inclusion criteria* Patients with urinary retention: 1. Postvoid residual volume > 400 mL OR Indwelling catheter or suprapubic tube OR	*PVP* Laser: 80 Watt KTP/532 nm laser (GreenLight PV™) Surgeon experience: not described	*Primary outcomes* (Follow-up: 1, 3, 6, and 12 months) 1. Maximum urinary flow rate 2. Postvoiding residual volume 3. IPPS score *Secondary outcomes* (Follow-up: discharge) 1. Prostate Specific Antigen (PSA) levels *Perioperative outcomes* 1. Operating time (minutes) 2. Length of catheterization (hours)	Grade: C Level of evidence: 4

Study authors (year published)	Methods	Patients	Intervention	Outcomes	Study Quality*
		Clean intermittent catheterization at least once daily 2. Failed voiding trial 3. Taking at least 1 medication for BPH		3. Length of hospital stay (hours) *Adverse events/complications*	
Ruszat et al (2006)	Case series - prospective - consecutive patients - 21 patients lost to follow-up Country: Switzerland	Number of patients: 183 - refractory urinary retention: 70 - no refractory urinary retention: 113 Mean age: 71.7 years Age range: 46 years to 95 years *Inclusion criteria* 1. Maximum urinary flow rate (Q_{max}) $\leq$ 15 mL/s OR Postvoid residual volume > 300 mL 2. IPPS > 7 *Exclusion criteria* 1. Prostate cancer	*PVP* Laser: 80 Watt KTP/532 nm laser (GreenLight PV™) Surgeon experience: not described	*Primary outcomes* (Follow-up: 1, 3, 6, 12, and 24 months) 1. Maximum urinary flow rate 2. Postvoiding residual volume 3. IPSS score 4. IPPS QoL scores *Perioperative outcomes* 1. Operating time (minutes) 2. Length of catheterization (hours) 3. Length of hospital stay (hours) 4. Change in hemoglobin (g/dL) *Adverse events/complications*	Grade: C Level of evidence: 4

* Based on the Oxford Centre for Evidence-Based Medicine Levels of Evidence (http://www.cebm.net/levels_of_evidence.asp#levels)

Table 5.2 Summary of excluded studies

Study authors (year published)	Main reason for exclusion
Bachmann et al (2003) Abstract only	Patients already included in study by Bachmann et al (see Table 2.1) - presents early results from 1 centre involved in a bi-centre prospective study
Malek et al (2003) Abstract only	Includes patients treated with 60 Watt KTP laser
Mattioli (2003) Abstract only	Includes patients treated with 60 Watt KTP laser
Nseyo et al (2003) Abstract only	Patients already included in study by Te et al (see Table 2.1) - presents early results of a single centre involved in a multi-centre prospective study
Sandhu et al (2003) Abstract only	Patients already included in study by Sandhu et al (see Table 2.1) - presents early results of same clinical series
Te et al (2003) Abstract only	Patients already included in study by Te et al (see Table 2.1) - presents early results of a multi-centre prospective study
Ulchaker et al (2003) Abstract only	Patients already included in study by Te et al (see Table 2.1) - presents early results of multi-centre prospective study
Ulchaker et al (2003) Abstract only	Patients already included in study by Te et al (see Table 2.1) - presents 1 year follow-up results of multi-centre prospective study
Bachmann et al (2004) Abstract only	Patients already included in study by Bachmann et al (see Table 2.1) - presents 6 months follow-up results from 1 centre involved in a bi-centre prospective study
Malloy et al (2004) Abstract only	Patients already included in study by Te et al (see Table 2.1) - presents 2 year follow-up results of 10 patients in multi-centre prospective study
Reich et al (2004)	Patients already included in study by Bachmann et al (see Table 2.1) - presents early results of a bi-centre prospective study
Sandhu et al (2004)	Patients already included in study by Te et al (see Table 2.1) - presents results from 1 centre involved in a multi-centre prospective study
Sulser et al (2004)	Patients already included in study by Ruszat et al (see Table 2.1) - earlier report on same clinical series
Te et al (2004) Abstract only	Transurethral electrovaporization of the prostate used as the comparator
Bachmann et al (2005)	Patients already included in study by Bachmann et al (see Table 2.1) - presents results from 1 centre involved in a bi-centre study

Table 5.2 Summary of excluded studies

Study authors (year published)	Main reason for exclusion
Fu et al (2005)	Patients already included in study by Fu et al (see Table 2.1) - earlier report on same clinical series
Kumar (2005)	Includes patients with prostate cancer
Malek et al (2005)	Includes patients treated with 60 Watt KTP laser
Sandhu et al (2005)	Patients already included in study by Te et al (see Table 2.1) - presents sub-group analysis of patients receiving anticoagulants
Ruszat et al (2006)	Patients already included in study by Ruszat et al (see Table 2.1) - presents sub-group analysis of patients receiving anticoagulants
Ruszat et al (2006) Abstract only	Patients already included in study by Ruszat et al (see Table 2.1) - presents results of sub-group analysis comparing patients with prostate volumes > 80 cm^3 to those with prostate volumes $\leq$ 80 cm^3
Lingeman et al (2006)	Currently recruiting RCT using Holmium Laser Ablation of the Prostate (HoLAP) as the comparator
Te et al (2006)	Patients already included in study by Te et al (see Table 2.1) - presents sub-group analysis of patients receiving anticoagulants
Te et al (2006)	Patients already included in study by Te et al (see Table 2.1) - presents stratified analysis of results according total prostate specific antigen levels before treatment

Table 5.3 Summary of adverse events/complications reported in patients who underwent PVP

Study authors (year published)	Reported adverse events/complications (% of study sample)												
	No. of patients	Acute renal failure	Urinary retention	Clot retention	Hematuria*	Dysuria*	Urinary tract infection	Incontinence (stress or urge)	Stricture (bladder neck or urethral) or bladder neck contracture	Bladder stenosis	Epididymitis	Erectile dysfunction	Retrograde ejaculation†
Comparative studies													
Bachmann et al (2005)	64	1 (1.6%)	5 (7.8%)	0 (0.0%)	0 (0.0%)	7 (10.9%)	7 (10.9%)	0 (0.0%)	5 (7.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	not available
Bouchier-Hayes et al (2006)	38	0 (0.0%)	3 (7.8%)	0 (0.0%)	0 (0.0%)	8 (21.1%)	2 (5.3%)	0 (0.0%)	0 (0.0%)	5 (13.2%)	0 (0.0%)	not available	not available
Pooled total	**102**	**1 (0.98%)**	**8 (7.8%)**	**0 (0.0%)**	**0 (0.0%)**	**15 (14.7%)**	**9 (8.8%)**	**0 (0.0%)**	**5 (4.9%)**	**5 (4.9%)**	**0 (0.0%)**	-	-
Non-comparative studies													
Hai and Malek (2003)	10	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (10.0%)	2 (20.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	not available	not available
Sandhu et al (2004)	64	0 (0.0%)	2 (3.1%)	1 (1.6%)	0 (0.0%)	0 (0.0%)	1 (1.6%)	0 (0.0%)	2 (3.1%)	0 (0.0%)	0 (0.0%)	not available	not available
Te et al (2004)	139	0 (0.0%)	7 (5.0%)	1 (0.7%)	12 (8.6%)	13 (9.4%)	3 (2.2%)	9 (6.5%)	3 (2.2%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	27 (36%)
Barber et al (2004)	30	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.7%)	0 (0.0%)	2 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	10 (55.6%)
Fu et al (2005)	196	0 (0.0%)	0 (0.0%)	1 (0.5%)	5 (2.6%)	3 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	not available
Park & Ha (2005)	82	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (3.7%)	7 (8.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	not available	not available
Sarica (2005)	240	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (2.9%)	26 (10.8%)	0 (0.0%)	8 (3.3%)	2 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	- (55%)
Volkan et al (2005)	186	0 (0.0%)	0 (0.0%)	2 (1.1%)	10 (5.4%)	55 (29.6%)	12 (6.5%)	0 (0.0%)	2 (1.1%)	0 (0.0%)	0 (0.0%)	not available	not available
Han et al (2006)	104	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.9%)	0 (0.0%)	0 (0.0%)	2 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	12 (11.6%)
Monoski et al (2006)	40	0 (0.0%)	3 (7.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (7.5%)	0 (0.0%)	0 (0.0%)	not available	not available
Ruszat et al (2006)	183	1 (0.5%)	0 (0.0%)	0 (0.0%)	2 (1.1%)	10 (5.5%)	8 (4.4%)	3 (1.6%)	10 (5.5%)	0 (0.0%)	0 (0.0%)	not available	not available
Pooled total	**1,274**	**1 (0.1%)**	**12 (0.9%)**	**5 (0.4%)**	**40 (3.1%)**	**119 (9.3%)**	**26 (2.0%)**	**20 (1.6%)**	**26 (2.0%)**	**0 (0.0%)**	**1 (0.1%)**	-	-
Published values for TURP‡		not available	**4.9%**	**6.8%**	**6.0%**	**12.0%**	**4.7%**	**1.3%**	**3.6%**	**3.4%§**	**1.3%**	**4.9%**	**52.8%**

* Mild to moderate – no medical treatment required

† Denominator comprised of self-reported sexually active men prior to surgery

‡ From published clinical practice guidelines (American Urological Association, 2003)

Table 5.4 Adverse events/complications following PVP compared with TURP

Adverse event/ complication	Patients with adverse event (n) in study group (N) PVP n/N	TURP n/N	Pooled Effect Estimate Relative Risk (95% CI)	Favors PVP	Favors TURP
*Severe bleeding**					
Non-RCT	0/64	4/37	0.11 (0.01 to 1.99)		Neither
RCT	0/38	4/38	Not statistically significant		
Acute renal failure					
Non-RCT	0/64	0/37	3.00 (0.01 to 1.99)		Neither
RCT	1/38	0/38	Not statistically significant		
Capsule perforation					
Non-RCT	0/64	0/37	0.33 (0.01 to 7.93)		Neither
RCT	0/38	1/38	Not statistically significant		
Urinary retention					
Non-RCT	5/64	1/37	2.94 (0.64 to 13.56)		Neither
RCT	3/38	1/38	Not statistically significant		
Clot retention					
Non-RCT	0/64	1/37	0.09 (0.01 to 0.72)	✓	
RCT	0/38	10/38			
Dysuria†					
Non-RCT	7/64	4/37	1.10 (0.53 to 2.26)		Neither
RCT	2/38	3/38	Not statistically significant		
Urinary tract infection					
Non-RCT	7/64	4/37	0.89 (0.34 to 2.33)		Neither
RCT	2/38	3/38	Not statistically significant		
Urethral stricture					
Non-RCT	5/64	1/37	0.59 (0.02 to 18.42)		Neither
RCT	0/38	5/38	Not statistically significant		
Bladder stenosis					
Non-RCT	0/64	0/37	1.67 (0.43 to 6.49)		Neither
RCT	5/38	3/38	Not statistically significant		
TUR syndrome					
Non-RCT	0/64	0/37	0.33 (0.01 to 7.93)		Neither
RCT	0/38	1/38	Not statistically significant		
Erectile dysfunction					
Non-RCT	0/64	0/37	0.19 (0.01 to 4.66)		Neither
RCT	no data available	no data available	Not statistically significant		
Recatheterization‡					
Non-RCT	0/64	0/37	0.17 (0.02 to 1.32)		Neither
RCT	1/38	6/38	Not statistically significant		
Transfusion					
Non-RCT	0/64	0/37	0.33 (0.01 to 7.93)		Neither
RCT	0/38	1/38	Not statistically significant		

Non-RCT= Study by Bachmann et al
RCT = Study by Bouchier-Hayes et al
*Severe bleeding requiring intraoperative management or abortion of the procedure
†Mild to moderate – no medical treatment required
‡Recatheterization for > 48 hours due to failed trial of voiding or secondary hemorrhage

Table 5.5 Operative outcomes following PVP from included non-comparative studies

	Patient Characteristics													
	Age (years)		Preoperative prostate volume (ml)		Operating time (minutes)		Length of hospital stay (hours)		Length of catheterization (hours)		Change in hemoglobin (g/dL)		Reoperation within follow-up period (%)†	
Study	Mean (SD)‡	Range	Mean (SD)‡	Range	Mean (SD)‡	Range	Mean (SD)‡	Range	Mean (SD)‡	Range	Mean (SD)‡	Range	N (%)	length of follow-up (months)
Hai and Malek (2003)	64.1 (7.6)	58 - 73	41.4 (18.5)	24 - 76.3	19.8 (4.9)	14 - 28	not available	not available	17.2 (9.6)	0 - 28	not available	not available	0 (0.0)	12
Mattioli et al (2003)	not available	48 - 85	not available	not available	not available	15 - 60	not available	not available	not available	3 - 6	not available	not available	0 (0.0)	12
Sandhu et al (2004)	70.1 (10.7)	not available	101 (40)	not available	122.9 (23.3)	53-193	< 23 hrs	not available	not available	0 - 23	not available	not available	3 (4.7)	12
Te et al (2004)	67.7 (8.7)	45 - 88	54.6 (31.7)	21 - 174	38.7 (23.3)	9 - 140	119 patients ≤ 23 hrs 27 patients 24-72 hrs	not available	14.1 (14.7)	0 - 72	not available	not available	0 (0.0)	12
Barber et al (2004)	66	not available	60	not available	not available	not available	18 patients < 4 hrs 12 patients < 24_ hrs	not available	not available	0 - 15	not available	not available	0 (0.0)	6
Fu et al (2005)	75	50 - 92	63.5 (16.8)	30 – 336	45.2 (18.5)	15 - 210	not available	not available	43.2 (21.6)	not available	- 1.3 g/dL*	not available	0 (0.0)	3
Park & Ha (2005)	65.6	51 - 86	39.7	22 - 75	24.7	15 - 45	not available	not available	17.2	2 - 24	not available	not available	0 (0.0)	6
Sarica (2005)	67.4	46 - 83	52.1	28 - 120	45	25 - 90	< 24 hrs	not available	12.2 (6.8)	6 - 24	not available	not available	0 (0.0)	12
Volkan et al (2005)	66 (8)	47 - 90	48.1 (13.2)	17 - 94	57 (17)	10 - 120	14.4 (1.2)	10.5 - 17	7.6 (0.9)	6 - 13	-0.6 g/dL*	not available	2 (1.1)	12
Han et al (2006)	44.9	23 - 95	47.6 (23.9)	not available	44.9	23 - 95	4.8 (10.3)	not available	27.1 (11.0)	not available	not available	not available	2 (2.5)	6
Monoski et al (2006)	not available	not available	110.7 (47.9)	not available	137.3 (63.4)	not available	< 23 hrs	not available	not available	0 - 23	not available	not available	3 (7.5)	12
Ruszat et al (2006)	71.7 (9.5)	46 - 95	56.1 (31.0)	10 - 180	59.5 (26.4)	10 - 160	129.6 (57.6)	72 - 384	43.2 (45.6)	24 - 240	not available	not available	15 (8.2)	24

†Standard deviations reported where available

*Difference between pre- and post-operative values not statistically significant

‡Reoperation for recurrent symptoms – re-PVP, TURP, urethrotomy, or bladder neck incision

Table 5.6 Operative outcomes following PVP versus TURP from included comparative studies

Parameter	Intervention: PVP Mean (SD)	Intervention: TURP Mean (SD)	Pooled Effect Estimate Weighted Mean Difference (95% CI)*	Favors PVP	Favors TURP
Age (years)			Not applicable		
Non-RCT	71.0 (9.3)	68.7 (7.9)	p-value > 0.05		Not applicable
RCT	65.23 (range: 51-81)	66.23 (range: 55-80)	p-value > 0.05		
Preoperative prostate volume (cm^3)			Not applicable		
Non-RCT	65.1 (36.9)	48.9 (21.2)	p-value > 0.05		Not applicable
RCT	42.44 (range: 16.5-82.6)	33.22 (range: 15.4-67.5)	p-value > 0.05		
Operating time (minutes)			Not calculable		
Non-RCT	59.6 (24.4)	49.4 (16.0)	p-value = 0.05 (ns)		Neither
RCT	30.24	31.33	p-value > 0.05 (ns)		
Length of hospital stay (days)					
Non-RCT	5.5 (2.7)	7.1 (1.8)	-2.08 (-2.73 to -1.42)	✓	
RCT	1.08 (0.28)	3.39 (1.17)			
Length of catheterization (hours)					
Non-RCT	43.2 (43.2)	72 (36)	-31.29 (-39.72 to -22.87)	✓	
RCT	12.2 (8.6)	44.5 (30.2)			
Blood loss (change in hemoglobin (g/dL))			Not calculable		
Non-RCT	0.7	1.7	p-value = 0.027	✓	
RCT	0.5	1.5	p-value <0.0005		
Reoperation within follow-up period	Number of patients	Number of patients	Relative Risk (95% CI)		
Non-RCT	0	0	4.87 (0.24 – 98.18) (ns)		Neither
RCT	2	0			

non-RCT= Study by Bachmann et al
RCT = Study by Bouchier-Hayes et al
*Weighted mean differences were calculated where reported data permitted
ns = not statistically significant

Table 5.11 Mean changes in functional outcomes after PVP versus TURP at first post-discharge follow-up visit from included comparative studies

	Intervention Mean difference between pre- and post- operative values				
Functional outcome	**PVP**	**TURP**	**P-value for the difference between groups**	**Favors PVP**	**Favors TURP**
Peak voiding flow (Q_{max})					
Increase in $Q_{max.}$ (mL/sec)					
Non-RCT†	10.7	12.6	> 0.05 (ns)	Neither	
RCT‡	12.0	8.6	> 0.05 (ns)	Neither	
% improvement					
Non-RCT	155.0%	183.0%	> 0.05 (ns)	Neither	
RCT	167.4%	149.0%	> 0.05 (ns)	Neither	
Postvoiding residual volume (V_{res})					
Decrease in V_{res} (mL)					
Non-RCT	129.0	93.9	> 0.05 (ns)	Neither	
RCT	125.0	86.0	> 0.05 (ns)	Neither	
% improvement					
Non-RCT	88.0%	77.8%	> 0.05 (ns)	Neither	
RCT	Not available	Not available	-	-	
International Prostate Symptom Score (IPPS)					
Decrease in IPSS*					
Non-RCT	9.5	6.7	> 0.05 (ns)	Neither	
RCT	14.0	12.9	> 0.05 (ns)	Neither	
% improvement					
Non-RCT	52.5%	38.7%	> 0.05 (ns)	Neither	
RCT	49.8%	50.2%	> 0.05 (ns)	Neither	
Quality of Life (QoL) Score					
Decrease in QoL score*					
Non-RCT	1.7	1.3	> 0.05 (ns)	Neither	
RCT	2.7	2.9	> 0.05 (ns)	Neither	
% improvement					
Non-RCT	51.5%	38.2%	> 0.05 (ns)	Neither	
RCT	Not available	Not available	-	-	

*Decrease in IPPS or QoL score indicates deduction in symptoms or increase in quality of life
†First post-discharge follow-up visit: 4 weeks
‡First post-discharge follow-up visit: 6 weeks
ns = not statistically significant

Table 5.7 Change in peak urinary flow (Q_{max}) after PVP during follow-up across studies

Study		Increase in Q_{max} (mL/sec) from pre-operative values					
		Discharge	**1 month**	**3 months**	**6 months**	**12 months**	**24 months**
Comparative studies							
Bachmann et al (2005)	Mean increase	8.9	10.7	10.6	11.2	Not available	Not available
	% cumulative improvement	129.0%	155.0%	153.6%	162.3%	Not available	Not available
	Statistical significance (p-value)*	<0.0001	<0.0005			Not available	Not available
Bouchier-Hayes et al (2006)	Mean increase	Not available	12.0†	Not available	Not available	Not available	Not available
	% cumulative improvement	Not available	167.4%†	Not available	Not available	Not available	Not available
	Statistical significance (p-value)*	Not available	p-value = 0.009	Not available	Not available	Not available	Not available
Pooled weighted mean increase (mL/sec)		**8.9**	**Not calculable**	**10.6**	**11.2**	**-**	**-**
Non-comparative studies							
Hai and Malek (2003)	Mean increase	Not available	11.7	15.3	19.1	20.4	Not available
	% cumulative improvement	Not available	113.6%	148.5%	185.4%	198.1%	Not available
	Statistical significance (p-value)*	Not available	<0.0001	<0.0001	<0.0001	<0.0001	Not available
Mattioli et al (2003)	Mean increase	Not available	Not available	Not available	Not available	16.0	Not available
	% cumulative improvement	Not available	Not available	Not available	Not available	197.5%	Not available
	Statistical significance (p-value)*	Not available	Not available	Not available	Not available	Not available	Not available
Sandhu et al (2004)	Mean increase	Not available	8.5	8.3	12.1	11.0	Not available
	% cumulative improvement	Not available	107.6%	105.1%	153.2%	139.2%	Not available
	Statistical significance (p-value)*	Not available	<0.001	<0.001	<0.001	<0.001	Not available
Te et al (2004)	Mean increase	Not available	11.7	12.8	14.0	14.8	Not available
	% cumulative improvement	Not available	150.0%	164.1%	179.4%	189.7%	Not available
	Statistical significance (p-value)*	Not available	<0.05	<0.05	<0.05	<0.05	Not available
Barber et al (2004)	Mean increase	Not available	Not available	Not available	11.2	Not available	Not available
	% cumulative improvement	Not available	Not available	Not available	136.6%	Not available	Not available
	Statistical significance (p-value)*	Not available	Not available	Not available	Not available	Not available	Not available
Fu et al (2005)	Mean increase	Not available	Not available	12.9	Not available	Not available	Not available
	% cumulative improvement	Not available	Not available	192.5%	Not available	Not available	Not available
	Statistical significance (p-value)*	Not available	Not available	<0.05	Not available	Not available	Not available
Park & Ha (2005)	Mean increase	Not available	Not available	Not available	8.7	Not available	Not available
	% cumulative improvement	Not available	Not available	Not available	110%	Not available	Not available
	Statistical significance (p-value)*	Not available	Not available	Not available	<0.01	Not available	Not available
Sarica (2005)	Mean increase	6.7	Not available	Not available	16.7	18.2	Not available
	% cumulative improvement	84.8%	Not available	Not available	211.4%	230.4%	Not available
	Statistical significance (p-value)*	<0.001	Not available	Not available	<0.001	<0.001	Not available
Volkan et al (2005)	Mean increase	Not available	7.7	7.7	Not available	Not available	Not available
	% cumulative improvement	Not available	108.5%	108.5%	Not available	Not available	Not available
	Statistical significance (p-value)*	Not available	<0.0001	<0.0001	Not available	Not available	Not available
Han et al (2006)	Mean increase	Not available	8.8	8.3	6.5	Not available	Not available
	% cumulative improvement	Not available	106.4%	99.6%	78.8%	Not available	Not available
	Statistical significance (p-value)*	Not available	<0.001	<0.001	<0.001	Not available	Not available
Monoski et al (2006)	Mean increase	Not available	9.4	8.0	12.3	11.5	Not available
	% cumulative improvement	Not available	139.8%	114.7%	188.2%	174.8%	Not available

Table 5.7 Change in peak urinary flow (Q_{max}) after PVP during follow-up across studies

Study		Increase in Q_{max} (mL/sec) from pre-operative values					
		Discharge	**1 month**	**3 months**	**6 months**	**12 months**	**24 months**
	Statistical significance (p-value)*	Not available	<0.05	<0.05	<0.05	<0.05	Not available
Ruszat et al (2006)	Mean increase	7.5	11.4	12.1	12.0	12.9	14.4
	% cumulative improvement	105.1%	160.7%	170.7%	168.6%	182.2%	203.1
	Statistical significance (p-value)*	Not available	Not available	Not available	Not available	Not available	Not available
Pooled weighted mean increase (mL/sec)		**7.0**	**9.7**	**10.5**	**13.2**	**16.4**	**14.4**
Published values for TURP (mean increase in Q_{max})‡				**3-9 months: 10.5**		**12 months: 10.8**	**16 months: 8.1**

*Statistical significance when compared with preoperative or baseline value
†After 6 weeks follow-up
‡From published clinical practice guidelines (American Urological Association, 2003)

Table 5.8 Change in post-voiding residual volume (V_{res}) after PVP during follow-up across included studies

Study		Decrease in V_{res} (mL) from pre-operative values					
		Discharge	**1 month**	**3 months**	**6 months**	**12 months**	**24 months**
Comparative studies							
Bachmann et al (2005)	Mean decrease	74.6	129.0	133.0	133.2	Not available	Not available
	% cumulative improvement	51.1%	88.3%	91.0%	91.2%	Not available	Not available
	Statistical significance (p-value)*	<0.001	<0.001	0.048	0.025	Not available	Not available
Bouchier-Hayes et al (2006)	Mean decrease	Not available	125.0†	Not available	Not available	Not available	Not available
	% cumulative improvement	Not available	85.0%†	Not available	Not available	Not available	Not available
	Statistical significance (p-value)*	Not available	<0.0005	Not available	Not available	Not available	Not available
Pooled weighted mean decrease (mL/)		**74.6**	**Not calculable**	**133.0**	**133.2**	**-**	**-**
Non-comparative studies							
Hai and Malek (2003)	Mean decrease	Not available	117.2	132.2	133.6	134.6	Not available
	% cumulative improvement	Not available	85.2%	96.1%	97.1%	97.8%	Not available
	Statistical significance (p-value)*	Not available	0.005	0.003	0.001	0.001	Not available
Mattioli et al (2003)	Mean decrease	Not available	Not available	Not available	Not available	98.5	Not available
	% cumulative improvement	Not available	Not available	Not available	Not available	96.6%	Not available
	Statistical significance (p-value)*	Not available	Not available	Not available	Not available	Not available	Not available
Sandhu et al (2004)	Mean decrease	Not available	111.0	111.0	122.0	80.0	Not available
	% cumulative improvement	Not available	58.7%	58.7%	64.6%	42.3%	Not available
	Statistical significance (p-value)*	Not available	<0.001	<0.001	<0.001	0.07	Not available
Te et al (2004)	Mean decrease	Not available	78.7	88.6	88.2	89.5	Not available
	% cumulative improvement	Not available	68.9%	77.5%	77.2%	78.3%	Not available
	Statistical significance (p-value)*	Not available	<0.05	<0.05	<0.05	<0.05	Not available
Barber et al (2004)	Mean decrease	Not available	Not available	Not available	88.5	Not available	Not available
	% cumulative improvement	Not available	Not available	Not available	75.3%	Not available	Not available
	Statistical significance (p-value)*	Not available	Not available	Not available	Not available	Not available	Not available
Fu et al (2005)	Mean decrease	Not available	Not available	132.6	Not available	Not available	Not available
	% cumulative improvement	Not available	Not available	83.7%	Not available	Not available	Not available
	Statistical significance (p-value)*	Not available	Not available	<0.05	Not available	Not available	Not available
Park & Ha (2005)	Mean decrease	Not available	Not available	Not available	62.2	Not available	Not available
	% cumulative improvement	Not available	Not available	Not available	98.0%	Not available	Not available
	Statistical significance (p-value)*	Not available	Not available	Not available	<0.01	Not available	Not available
Sarica (2005)	Mean decrease	Not available	Not available	Not available	93.0	129.4	Not available
	% cumulative improvement	Not available	Not available	Not available	63.9%	88.9%	Not available
	Statistical significance (p-value)*	Not available	Not available	Not available	<0.001	<0.001	Not available
Volkan et al (2005)	Mean decrease	Not available	Not available	127.1	Not available	Not available	Not available
	% cumulative improvement	Not available	Not available	93.5%	Not available	Not available	Not available
	Statistical significance (p-value)*	Not available	Not available	<0.0001	Not available	Not available	Not available
Han et al (2006)	Mean decrease	Not available	52.1	61.5	59.8	Not available	Not available
	% cumulative improvement	Not available	63.6%	75.0%	72.9%	Not available	Not available

Table 5.8 Change in post-voiding residual volume (V_{res}) after PVP during follow-up across included studies

Study		Decrease in V_{res} (mL) from pre-operative values					
		Discharge	**1 month**	**3 months**	**6 months**	**12 months**	**24 months**
	Statistical significance (p-value)*	Not available	<0.01	<0.01	<0.01	Not available	Not available
Monoski et al (2006)	Mean decrease	Not available	165.4	223.4	181.7	216.1	Not available
	% cumulative improvement	Not available	54.6%	68.2%	56.7%	65.7%	Not available
	Statistical significance (p-value)*	Not available	<0.05	<0.05	<0.05	<0.05	Not available
Ruszat et al (2006)	Mean decrease	137.5	184.5	189.2	173.2	177.5	199.1
	% cumulative improvement	58.7%	85.6%	87.1%	83.8%	83.0%	86.5%
	Statistical significance (p-value)*	Not available	Not available	Not available	Not available	Not available	Not available
Pooled weighted mean decrease (mL) (% improvement)‡		**137.5 (58.7%)**	**112.2 (70.5%)**	**117.7 (76.2%)**	**103.3 (74.4%)**	**114.9 (76.2%)**	**199.1 (86.5%)**
Published values for TURP (mean decrease (mL) and % improvement)‡				**3 months: 44.7 (44.0%)**	**Not available**	**12 months: 52.2 (51.0%)**	**24 months: 69.2 (68.0%)**

*Statistical significance when compared with preoperative or baseline value
†After 6 weeks follow-up
‡From published meta-analyses

Table 5.9 Change in IPPS / AUA symptom score after PVP during follow-up across included studies

Study		Decrease in score from pre-operative values					
		Discharge	**1 month**	**3 months**	**6 months**	**12 months**	**24 months**
Comparative studies							
Bachmann et al (2005)	Mean decrease*	9.1	9.5	11.4	12.9	Not available	Not available
	% cumulative improvement	50.3%	52.5%	63.0%	71.3%	Not available	Not available
	Statistical significance (p-value) §	<0.001	<0.001	<0.001	<0.001	Not available	Not available
Bouchier-Hayes et al (2006)	Mean decrease*	Not available	14.0	Not available	Not available	Not available	Not available
	% cumulative improvement	Not available	49.8%	Not available	Not available	Not available	Not available
	Statistical significance (p-value) §	Not available	<0.000001	Not available	Not available	Not available	Not available
Pooled weighted mean decrease in score (% improvement)		**9.1 (50.3%)**	**11.4 (66.5%)**	**11.4 (63.0%)**	**12.9 (71.3%)**	-	-
Non-comparative studies							
Hai and Malek (2003)	Mean decrease*	Not available	16.8	17.9	19.8	20.6	Not available
	% cumulative improvement	Not available	72.4%	77.2%	85.3%	88.8%	Not available
	Statistical significance (p-value) §	Not available	<0.0001	<0.0001	<0.0001	<0.0001	Not available
Mattioli et al (2003)	Mean decrease*	Not available	Not available	Not available	Not available	10.4	Not available
	% cumulative improvement	Not available	Not available	Not available	Not available	52.0%	Not available
	Statistical significance (p-value) §	Not available	Not available	Not available	Not available	Not available	Not available
Sandhu et al (2004)	Mean decrease*	Not available	8.5	9.8	11.2	11.7	Not available
	% cumulative improvement	Not available	46.2%	53.3%	60.9%	63.6	Not available
	Statistical significance (p-value) §	Not available	<0.001	<0.001	<0.001	<0.001	Not available
Te et al (2004)	Mean decrease*	Not available	16.0	18.0	18.9	19.7	Not available
	% cumulative improvement	Not available	67.0%	75%	79.0%	82.0%	Not available
	Statistical significance (p-value) §	Not available	<0.05	<0.05	<0.05	<0.05	Not available
Barber et al (2004)	Mean decrease*	Not available	Not available	Not available	15.4	Not available	Not available
	% cumulative improvement	Not available	Not available	Not available	68.8%	Not available	Not available
	Statistical significance (p-value) §	Not available	Not available	Not available	Not available	Not available	Not available
Fu et al (2005)	Mean decrease*	Not available	Not available	20.9	Not available	Not available	Not available
	% cumulative improvement	Not available	Not available	78.6%	Not available	Not available	Not available
	Statistical significance (p-value) §	Not available	Not available	<0.05	Not available	Not available	Not available
Park & Ha (2005)	Mean decrease*	Not available	Not available	Not available	15.7	Not available	Not available
	% cumulative improvement	Not available	Not available	Not available	71.0%	Not available	Not available
	Statistical significance (p-value) §	Not available	Not available	Not available	<0.01	Not available	Not available
Sarica (2005)	Mean decrease*	Not available	Not available	Not available	14.4	17.3	Not available
	% cumulative improvement	Not available	Not available	Not available	63.7%	76.5%	Not available
	Statistical significance (p-value) §	Not available	Not available	Not available	<0.001	<0.001	Not available
Volkan et al (2005)	Mean decrease*	Not available	Not available	4.7	12.1	12.0	Not available
	% cumulative improvement	Not available	Not available	25.0%	64.4%	63.8%	Not available
	Statistical significance (p-value) §	Not available	Not available	<0.0001	<0.0001	<0.0001	Not available
Han et al (2006)	Mean decrease*	Not available	10.4	12.6	11.4	Not available	Not available
	% cumulative improvement	Not available	46.3%	56.2%	51.1%	Not available	Not available
	Statistical significance (p-value) §	Not available	<0.001	<0.001	<0.001	Not available	Not available

Table 5.9 Change in IPPS / AUA symptom score after PVP during follow-up across included studies

Study		Decrease in score from pre-operative values					
		Discharge	**1 month**	**3 months**	**6 months**	**12 months**	**24 months**
Monoski et al (2006)	Mean decrease*	Not available	6.6	6.8	8.6	8.7	Not available
	% cumulative improvement	Not available	38.6%	39.9%	51.2%	51.6%	Not available
	Statistical significance (p-value) [§]	Not available	<0.05	<0.05	<0.05	<0.05	Not available
Ruszat et al (2006)	Mean decrease	7.7	7.9	10.2	11.6	11.4	11.6
	% cumulative improvement	44.2%	45.5%	57.9%	65.6%	64.8%	68.0%
	Statistical significance (p-value) [§]	Not available	Not available	Not available	Not available	Not available	Not available
Pooled weighted mean decrease in score (% improvement)		**7.7 (44.2%)**	**10.9 (51.8%)**	**13.1 (57.4%)**	**14.0 (66.4%)**	**14.7 (69.8%)**	**11.6 (68.0%)**
Published values for TURP (mean decrease in symptom score)[‡]				**3-9 months: 14.7**		**12 months: 14.8**	**16 months: 13.5**

*Decrease in IPPS or QoL score indicates deduction in symptoms or increase in quality of life
[§]Statistical significance when compared with preoperative or baseline value
[†]After 6 weeks follow-up
[‡] From published clinical practice guidelines (American Urological Association, 2003)

Table 5.10 Change in Quality of Life Score after PVP during follow-up across included studies

Study		Decrease in score from pre-operative values					
		Discharge	**1 month**	**3 months**	**6 months**	**12 months**	**24 months**
Comparative studies							
Bachmann et al (2005)	Mean decrease*	1.8	1.7	2.2	2.2	Not available	Not available
	% cumulative improvement	54.5%	51.5%	66.7%	66.7%	Not available	Not available
	Statistical significance (p-value) [§]	<0.001	<0.001	<0.001	<0.001	Not available	Not available
Bouchier-Hayes et al (2006)	Mean decrease*	Not available	2.65	Not available	Not available	Not available	Not available
	% cumulative improvement	Not available	Not calculable	Not available	Not available	Not available	Not available
	Statistical significance (p-value) [§]	Not available	<0.00005	Not available	Not available	Not available	Not available
Pooled weighted mean decrease in score (% improvement)		**1.8 (54.5%)**	**2.1 Not calculable**	**2.2 (66.7%)**	**2.2 (66.7%)**	-	-
Non-comparative studies							
Hai and Malek (2003)	Mean decrease*	Not available	2.7	3.5	3.9	3.9	Not available
	% cumulative improvement	Not available	62.8%	81.9%	90.7%	90.7%	Not available
	Statistical significance (p-value) [§]	Not available	<0.0001	<0.0001	<0.0001	<0.0001	Not available
Te et al (2004)	Mean decrease*	Not available	2.2	2.8	3.1	3.3	Not available
	% cumulative improvement	Not available	51.2%	65.1%	72.1%	76.7%	Not available
	Statistical significance (p-value) [§]	Not available	<0.05	<0.05	<0.05	<0.05	Not available
Barber et al (2004)	Mean decrease*	Not available	Not available	Not available	3.3	Not available	Not available
	% cumulative improvement	Not available	Not available	Not available	71.7%	Not available	Not available
	Statistical significance (p-value) [§]	Not available	Not available	Not available	Not available	Not available	Not available
Fu et al (2005)	Mean decrease*	Not available	Not available	4.1	Not available	Not available	Not available
	% cumulative improvement	Not available	Not available	71.9%	Not available	Not available	Not available
	Statistical significance (p-value) [§]	Not available	Not available	<0.05	Not available	Not available	Not available
Park & Ha (2005)	Mean decrease*	Not available	Not available	Not available	3.2	Not available	Not available
	% cumulative improvement	Not available	Not available	Not available	69.6%	Not available	Not available
	Statistical significance (p-value) [§]	Not available	Not available	Not available	<0.01	Not available	Not available
Ruszat et al (2006)	Mean decrease	1.7	1.8	2.3	2.5	2.4	2.4
	% cumulative improvement	48.6%	50.8%	65.0%	71.3%	69.6%	69.6%
	Statistical significance (p-value) [§]	Not available	Not available	Not available	Not available	Not available	Not available
Pooled weighted mean decrease in score (% improvement)		**1.7 (48.6%)**	**2.0 (51.4%)**	**3.3 (68.4%)**	**3.0 (65.6%)**	**3.0 (74.6%)**	**2.4 (69.6%)**
Published values for TURP (mean decrease in symptom score)[‡]				**3-9 months: 3.4**		**12 months: 3.3**	**16 months: 3.0**

*Decrease in IPPS or QoL score indicates a reduction in symptoms or increase in quality of life
[§]Statistical significance when compared with preoperative or baseline value
[†]After 6 weeks follow-up
[‡] From published clinical practice guidelines (American Urological Association, 2003)

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APPENDIX 1. Summary of direct and indirect medical costs over 5 years for patients receiving TURP between April 1, 1999 and March 31, 2005

Complication/Adverse event	Costed cases (n)	Average length of stay* (days)	Average cost per case† ($Cdn /case)	Diagnostic codes applied‡
Acute renal failure	4	7.5	Direct and indirect costs: $10,609.91 Physician fees: $281.79 **Total cost: $10,994.25**	ICD 9: 5849 (unspecified acute renal failure), 5845 (acute renal failure) ICD 10: N179 (acute renal failure)
Urinary retention	69	0.82	Direct and indirect costs: $566.2 Physician fees: $45.05 **Total cost:** $611.76	ICD 9: 78820 (unspecified retention of urine), 78829 (other specified retention of urine) ICD 10: R33 (unspecified retention of urine)
Clot retention	5	3.0	Direct and indirect costs: $2,691.69 Physician fees: $23.33 **Total cost: $2,815.02**	Inpatient admission AND ICD 9: 5997 (hematuria), 99812 (hematoma complicating a procedure) ICD 10: R310 or R318 (unspecified hematuria), T810 (hemorrhage and hematoma complicating a procedure)
Hematuria	52	1.0	Direct and indirect costs: $271.40 Physician fees: $51.48 **Total cost: $327.71**	ICD 9: 5997 (hematuria) ICD 10: R31 or R318 (unspecified hematuria), N029 (persistent hematuria)
Dysuria	1	1.0	Direct and indirect costs: $203.83 Physician fees: $40.40 **Total cost: $244.23**	ICD 9: 7881 (dysuria) ICD 10: R30 (dysuria)
Urinary tract infection	58	1.0	Direct and indirect costs: $359.09 Physician fees: $35.78 **Total cost: $394.87**	ICD 9: 5990 (UTI site not specified) ICD 10: N390 (UTI site not specified), T835 (infection due to prosthetic device in urinary system)
Incontinence	1	1.0	Direct and indirect costs: $52.79 Physician fees: $94.80 **Total cost: $147.59**	ICD 9: 7883 (urinary incontinence), 78830 (unspecified urinary incontinence), 78839 (other urge incontinence); 78831, 78832, 78833 ICD 10: R32 (unspecified urinary incontinence), N394 (other specified urinary incontinence)
Bladder neck contracture or	12	1.1	Direct and indirect costs: $1,493.71 Physician fees: $192.49	ICD 9: 5960 (bladder neck obstruction), 5968

Complication/Adverse event	Costed cases (n)	Average length of stay* (days)	Average cost per case† ($Cdn /case)	Diagnostic codes applied‡
stenosis			**Total cost: $1,686.20**	ICD 10: N320 (bladder neck obstruction/stenosis); Q64.3
Urethral stricture	9	1.3	Direct and indirect costs: $1,286.33 Physician fees: $40.92 **Total cost: $1,327.25**	ICD 9: 598 (urethral stricture), 5982 (postoperative urethral stricture), 5981, 5988, 5989 ICD 10: N390 (urethral stricture), N35.9, n99.1
Epididymitis	1	1.0	Direct and indirect costs: $92.93 Physician fees: $102.10 **Total cost: $195.03**	ICD 9: 604 (orchitis and epididymitis), 60490 (unspecified orchitis and epididymitis) ICD 10: N45 (orchitis and epididymitis)
Erectile dysfunction	2	2.0	Direct and indirect costs: $1,183.46 Physician fees: $127.03 **Total cost: $1,310.49**	ICD 9: 60784 (impotence of organic origin), 60782 (vascular disorders of penis), 6089, 6079 ICD 10: F522 (failure of genital response)
Bleeding	13	2.4	Direct and indirect costs: $2,129.25 Physician fees: $141.66 **Total cost: $2,270.91**	ICD 9: 2800 (anemia due to blood loss) 2859 (anemia), 99811 (hemorrhage complicating a procedure), 2851 (acute post hemorrhage anemia ICD 10: T81 (hemorrhage or hematoma complicating a procedure), D539 (anemia)
TUR syndrome	Not available	Not available	Direct and indirect costs: not available Physician fees: not available **Total cost:** not available	Not available
Re-operation	46	2.0	Direct and indirect costs: $2,196.0 Physician fees: $353.44 **Total cost: $2,549.44**	ICD 9: 6029 (TURP) ICD 10: 1QT87BA (TURP)

* Based on data from Alberta Health and Wellness MORB (in-patient) database and ACCS (ambulatory care) database
† Based on actual amounts paid by Alberta Health and Wellness for each relevant visit Physician fees were extracted from the physician claims database.
‡ Diagnostic codes used to initially identify relevant visits according to 'most responsible diagnosis'. Codes were selected with expert advice from a urologist and medical transcriptionist. Final decisions on included visits were based on a manual review of each potentially relevant record

APPENDIX 2. American Urological Association Symptom Index for Benign Prostatic Hyperplasia and the Disease Specific Quality of Life Question[34]

Questions	AUA BPH Symptom Score					
	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**
1. Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?	0	1	2	3	4	5
2. 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
3. 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
4. Over the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5
5. Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5
6. Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5
	None	**1 time**	**2 times**	**3 times**	**4 times**	**5 or more times**
7. Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?	0	1	2	3	4	5

Disease specific quality of life question

The International Prostate Symptom Score uses the same 7 questions as the AUA Symptom Index (presented above) with the addition of the following question (bother score), which is scored on a scale from 0 to 6 points (delighted to terrible):

"If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?"

APPENDIX 3. Oxford Centre for Evidence-based Medicine levels of evidence and grades of recommendation for studies of therapy[94]

Level of Evidence:

Level	Study design
1a	Systematic review with homogeneity of RCTs
1b	Individual RCT with narrow Confidence Interval
1c	All or none studies (where all patients died before the treatment became available)
2a	Systematic review with homogeneity of cohort studies
2b	Individual cohort study or low quality RCT (e.g., <80% follow-up)
2c	"Outcomes" research; Ecological studies
3a	Systematic review with homogeneity of case-control studies
3b	Individual case-control study
4	Case-series or poor quality cohort or case-control studies
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"

Grades of recommendation:

Grade	Levels of evidence
A (excellent)	Consistent level 1 studies
B (good)	Consistent level 2 or 3 studies or extrapolations from level 2 or 3 studies
C (fair)	Level 4 studies or extrapolations from level 2 or 3 studies
D (poor)	Level 5 evidence or troublingly inconsistent or inconclusive studies of any level