Cost-utility of minimally invasive therapies vs. pharmacotherapy as initial therapy for benign prostatic hyperplasia: A Canadian healthcare payer perspective

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KEY MESSAGES

- Compared to pharmacotherapy and to prostatic urethral lift procedure, initial treatment with water vapor thermal therapy was a more effective procedure over a patient's lifetime.
- Water vapor thermal therapy appears to be a cost-effective procedure.
- Water vapor thermal therapy may be an appropriate first-line alternative to pharmacotherapy for selected patients with prostate enlargement (≤80 cm^3) who seek faster improvement and no lifelong commitment to daily medications.

ABSTRACT

Introduction: Recently, minimally invasive surgical therapies (MISTs) have become an alternative to surgery or pharmacotherapy to manage benign prostatic hyperplasia (BPH). This study evaluated the cost-utility of water vapor thermal therapy (WVTT) and prostatic urethral lift (PUL) compared to pharmacotherapy as initial treatment for patients with moderate-to-severe BPH.

Methods: In this model-based economic evaluation, we simulated BPH progression in men (mean age 65 years, average International Prostate Symptom Score 16.6) over their lifetime and estimated healthcare

costs (from the Canadian healthcare payer perspective) per quality-adjusted life year (QALY), discounted at 1.5% annually. In the model, men could receive up to three lines of therapy: 1) initial pharmacotherapy with MIST as second-line, and TURP or pharmacotherapy as third-line; 2) initial MIST (WVTT or PUL) with MIST again, TURP or pharmacotherapy as second-line, and TURP as third-line. The model was populated using data from the published literature.
Results: The expected lifetime QALYs and costs were 15.50 QALYs and $14 626 for initial treatment with WVTT, 15.35 QALYs and $11 795 for pharmacotherapy followed by WVTT, 15.29 QALYs and $13 582 for pharmacotherapy followed by PUL, 15.29 QALYs and $19 151 for initial treatment with PUL. Strategies involving PUL procedures were dominated by strategies involving WVTT. The incremental cost per QALY gained was $18 873 for initial WVTT compared to initial pharmacotherapy followed by WVTT.
Conclusions: WVTT appears to be a cost-effective procedure and may be an appropriate first-line alternative to pharmacotherapy for patients with BPH and prostate volume less than 80 cm^3 who seek faster improvement and no lifelong commitment to daily medications.

INTRODUCTION

Lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) is highly prevalent condition managed by urologists in outpatient setting. In Canada about 20% of men seen by urologists are diagnosed with BPH.[1] Stepwise treatment options for LUTS/BPH include watchful waiting/lifestyle changes, pharmacotherapy (PhTx), and surgical interventions.[2] Therapeutic decision should be driven by the severity of the symptoms and patient preference.

PhTx is often considered as a first-line treatment for men with moderate to severe LUTS/BPH. However discontinuation rates are high, and in practice about two thirds of men may stop medications within 6 months of therapy.[3] Lack of compliance is often attributed to side effects, insufficient symptom relief, or unwillingness for a lifelong drug commitment. Although men may be willing to stay on PhTx to avoid surgery, drugs are expensive over longer periods of time.[4,5]

Transurethral resection of the prostate (TURP) is the gold standard for surgical treatment of LUTS/BPH, and it can improve symptoms and functional outcomes substantially.[2] However, the risk of post-operative complications including incontinence, urinary tract infection, erectile and ejaculatory dysfunction, acute urinary retention, and bladder neck contracture is significant.[6-8] TURP remains the most costly procedure as it requires hospitalization and is typically reserved for treatment of moderate-to-severe LUTS irresponsive to PhTx or for larger prostates.

Over the years, numerous less invasive surgical methods for the treatment of BPH have gained popularity, including non-ablative minimally invasive surgical treatments (MIST) such as water vapor thermal therapy (WVTT; Rezum® System, Boston Scientific, Marlborough, MA) and the prostatic urethral lift (PUL; UroLift System, Teleflex, Pleasanton, CA).[9-12] Both interventions could be performed in an outpatient setting.

WVTT and PUL are associated with fast and significant improvement in LUTS,[9-12] an advantage over PhTx. Procedure related adverse events (AEs) tend to be mild and resolve within few weeks.[9-12] Due to its non-ablative nature, MIST preserve sexual function better than standard surgeries. This sentiment cannot be understated as sexual function has been shown to be an important factor that influences patient preferences.[13] For individuals who do not want to commit for lifelong PhTx or who are seeking fast symptom relief and preservation of sexual function MIST could be considered as a potential alternative.

With the volume of evidence on these treatments steadily increasing, economic evaluations can help support decision-making with respect to the optimal use of MISTs for BPH management. While we have recently published an economic evaluation of MIST therapies from a US Medicare perspective,[5] an analysis from the Canadian healthcare payer perspective has not yet been undertaken. Since the economic evidence needs to be context-specific to be helpful in informing policy decisions,[14] we aimed to evaluate the cost-utility of PUL and WVTT compared to PhTx as initial treatment for men with moderate-to-severe BPH from the Canadian perspective.

METHODS

Details on methodology are published elsewhere.[5] Briefly, this cost–utility analysis evaluated the costs and quality-adjusted life-years (QALYs) of four common clinical pathways tailored for the management of BPH, from the Canadian healthcare perspective.

Population

Simulated individuals included men (a mean age (± standard deviation (SD)) of 65.0±7.0 years and an average (± SD) International Prostate Symptom Score (IPSS) of 16.6 ± 6.4, and a median (range) prostate volume 49 (30-80) cm^3) with moderate to severe symptoms, who are eligible for PhTx or MIST. The modeled individuals reflected characteristics of patients enrolled randomized control trials on PhTx, WVTT and PUL.[9,11,15]

Interventions

We modeled four common clinical pathways that an individual with moderate/severe BPH may undergo. Initial treatment options were limited to combination PhTx (alpha-blockers in combination with 5-alpha reductase inhibitors), WVTT or PUL. If symptoms did not resolve, simulated patients could receive up to two additional lines of therapy.

i) First line: PhTx→ Second line: PUL →Third line: TURP or PhTx;
ii) First line: PhTx→ Second line: WVTT→ Third line: TURP or PhTx;
iii) First line: WVTT→ Second line: repeat WVTT or PhTx or TURP→ Third line: TURP;
iv) First line: PUL → Second line: repeat PUL or PhTx or TURP→ Third line: TURP.

Outcomes

The study outcomes were direct healthcare costs (in 2020 CAD) and QALYs accumulated over lifetime. Both costs and QALYs were discounted at a 1.5% annual rate, in line with current Canadian economic evaluation guidelines.[16]

Model structure

We constructed an individual-level decision-analytic model (Figure 1) using TreeAge Pro 2021 R1.0.[17] Each simulated individual entered the model receiving either PhTx, WVTT or PUL, and was assigned starting age and IPSS scores based on random sampling from the corresponding distributions (Table 1). Natural history of BPH and clinical impact of interventions were modeled through 3-monthly changes in IPSS, mirroring three sub-states: mild BPH (IPSS < 8 points), moderate BPH (IPSS: 8 to 20 points), and severe BPH (IPSS ≥ 20 points). During any given 3-monthly cycle, a simulated individuals may transition between the three severity levels, defined through changes in IPSS score due to treatment or disease progression, develop treatment specific AEs, discontinue or switch treatment, receive re-treatment or die. Simulated individuals randomly transition through these temporary health states, with probabilities related to each intervention, and incur costs and utility weights associated with each event.

We assumed that individuals responsive to PhTx would experience maximum improvement in IPSS score by 12–27 weeks of treatment and remain stable thereafter [15]. Individuals receiving MIST or TURP would experience IPSS improvements over the cycle when the procedure was performed, would remain stable 5-8 years after TURP,[18,19] 2-5 years after the MIST (calibrated). Non-responsive individuals, those who discontinued PhTx due to AEs, and those beyond post-procedural stability period would experience worsening in IPSS score based on the natural history of BPH [20] and may receive subsequent lines of therapy if the decrease in IPSS score was <3 points relative to baseline. Due to scarce data on the effectiveness of repeated procedures, we conservatively assumed that the success rate of each procedure was independent of any previous procedures.

Clinical inputs

For individuals on combined PhTx, IPSS changes and AEs were derived from the CombAT trial.[15,21] For individuals who received WVTT or PUL, the IPSS was estimated using the mean difference in post-procedure IPSS relative to TURP from the network meta-analysis,[22] and safety data was retrieved from the respective clinical trials.[9-12,23] Patients on TURP were assumed to achieve an average decrease of 78% (*calibrated*) in IPSS relative to their pre-procedure score. Clinical inputs are summarized in Table 1 and Supplementary Table 1.

Utilities

Utility values for BPH severity levels and disutility values associated with procedures and related AEs (Supplementary Table 2) were obtained from the published literature.[21,24,25] Disutilities associated with procedures and AEs were assigned over the mean duration of recovery period and over 3 monthly cycle, respectively.[9,11,26]

Costs

The unit costs of PhTx and health services utilization were retrieved from the Ontario Drug Benefits program formulary and from the Ministry of Health and Long Term Care, Ontario Schedule of benefits.[27,28] Information on hospital costs for TURP were obtained from a retrospective cost analysis conducted at the Toronto Western Hospital, Toronto, Ontario.[29] We assumed that both WVTT and PUL occurred in an office setting, and incur same labor and overhead costs and similar to that of green light photoselective vaporization of the prostate (GL-PVP) day surgery cases.[29] Price estimates for patient supplies, such as single use delivery device for WVTT and implants for PUL (based on an average number of five implants[11]) were provided by clinical experts. The costs for acute urinary retention, bladder neck contracture/urethral stricture and blood transfusion, were obtained from the Canadian costing studies.[30,31] For non-Canadian sources (for TUR syndrome [32]), costs were converted to Canadian prices using purchasing power parity. All costs were inflated to the 2020 cost year (Table 1, Supplementary Table 3) using the consumer price index for health and personal care.[33]

Analysis

The model was calibrated and validated.[5] For the base case-analysis we simulated 250,000 patients over their lifetime. In the sensitivity analysis, we evaluated the thresholds of key model parameters (effectiveness, costs of MIT and duration of post-MIT symptom stability) that switch the cost-effectiveness results. Additionally, we assessed parameter uncertainty with a two-dimensional Monte Carlo simulation of 200 iterations with 2,500 simulated individuals each. Sampling distributions for transition probabilities, utility values and costs are provided in Table 1 and Supplementary Tables 1-3.

RESULTS

Over the lifetime horizon, initial treatment with WVTT was the most effective option, and was associated with 15.50 QALYs and $14,626 lifetime costs. The cumulative QALYs and lifetime costs were 15.35 QALYs and $11,795 for PhTx followed by WVTT, 15.29 QALYs and $13,582 for PhTx followed by PUL, and 15.29 QALYs and $19,151 for initial treatment with PUL (Table 2).

In the cost-utility analysis, strategies involving PUL procedures were dominated, i.e., generated fewer QALYs at higher cost (Table 2), by strategies involving WVTT procedures. After elimination of dominated strategies two strategies remained – initial WVTT and initial PhTx followed by WVTT. Compared to initial PhTx followed by WVTT, initial WVTT had an incremental cost of $2,831 and incremental QALYs of 0.15, resulting in an incremental cost-effectiveness ratio (ICER) of $18,873.

The cost breakdown revealed that the incremental cost was primarily driven by the costs of initial therapies, rather than by costs of subsequent therapies, AEs or BPH management (Table 3).

The threshold analysis showed that it would require 2.5-fold increase in cost of the WVTT, or substantial reduction in effectiveness (corresponding to the upper limit of the reported confidence interval), for initial WVTT be no longer cost-effective (Supplementary Table 4a). When the effectiveness for PUL was set to be similar to TURP, both PhTx followed by PUL (ICER = $8,176) and initial PUL (ICER = $12,670) became cost-effective, whereas initial WVTT became dominated strategy (Supplementary Table 4b). The presumed years of BPH symptom stability duration did not impact the results (Supplementary Table 4c)."

The probabilistic analysis showed the proportion of simulations being cost-effective at the commonly used $50,000 per QALY cost-effectiveness threshold: 71% for initial WVTT, 27.5% for initial PhTx followed by WVTT, and 1.5% for initial PhTx followed by PUL (Figure 2 and Figure 3).

DISCUSSION

This study evaluated the cost-utility of four clinical scenarios, offering WVTT, PUL or PhTx as initial therapy for BPH patients from a Canadian healthcare payer perspective. Our findings showed that initial treatment WVTT was the most effective option for men with moderate-to-severe BPH. Scenarios involving PUL, either as initial or as second line procedure were dominated, i.e., resulted in less QALY gain but at higher costs, relative to scenarios involving WVTT. Compared to initial PhTx followed by WVTT, initial WVTT deemed cost-effective considering 50,000 cost-effectiveness threshold. The results were primarily driven by differences in costs of initial procedures and re-treatment rates.

Our recently published study using US Medicare payer perspective demonstrated that among all four scenarios, initial WVTT was the most effective (13.05 QALYs) and the least costly option ($15,461),[5] contrasted with the current study, where initial WVTT was still the most effective, but also was more expensive than options involving initial PhTx. The costs differences between the studies were largely attributable to lower WVTT costs reported in the US ($2,261 USD vs $5,233 CAD), highlighting the importance of context in economic evaluations. The US Centers for Medicare & Medicaid Services has a specific billing code for WVTT (CPT 53854), while in Canada, there is no defined billing code for this procedure. In the current analysis we assumed that cost of WVTT would include costs for labor ($1,004 CAD), single use delivery device ($3,000 CAD) and facility overhead ($1,129 CAD).

The few economic analyses that evaluated WVTT vs PUL in men with moderate-to-severe BPH using the US Medicare perspective also indicated that WVTT is more effective and less costly,[34,35] while an evaluation from UK concluded that WVTT had comparable effectiveness but may offer cost-savings.[36] All these studies, however, had a limited time horizon of up to 4 years.

Our study has several strengths. We evaluated common clinical scenarios, given that in practice most men undergo several lifelong therapies up to surgical intervention. The model was based on natural history of BPH and considered a lifetime horizon, allowing to estimate the long-

term impact. Finally, our present study provides additional insights to the existing economic evidence on MIST.

However, our study also has limitations. Firstly, in the analysis we considered only combination PhTx, as the previous analysis of similar cohort of patients revealed that upfront monotherapies demonstrated negligible clinical and economic differences compared to combination therapies.[21] Secondly, even though we applied Canadian data where possible (e.g. costs), clinical assumptions were heavily based on the randomized controlled trials that may not be reflective of real-world data. Moreover, to date there are no studies directly comparing PhTx, WVTT or PUL that might create bias in evaluating their incremental effectiveness. However, the probabilistic sensitivity analyses showed that results were robust to the uncertainty of input parameters. Finally, several less invasive technologies are now available in Canadian market, such as prostatic artery embolization, aquablation, GL/PVP, and more recently emerged temporary implantable nitinol device (iTIND), but were excluded from the analysis to ensure model feasibility.

The emergence of MIST has the potential to shift the landscape of BPH management towards outpatient procedures. Our study suggests that WVTT is a cost-effective procedure, with an ICER of $18,873 that is below the commonly used $50,000 cost-effectiveness threshold. If WVTT became an alternative to first-line PhTx, the patient population seeking such treatment is likely to increase. Currently few centers in Canada offer WVTT. Further uptake of this technology would depend on its availability, clinician training and expertise with these devices.

To comment further on reimbursement recommendations one must take into consideration not only the cost-effectiveness but also the potential financial impact of new intervention on healthcare system. In a previous publication we showed that about half (54%) of patients stay on PhTx.[5] Even though we did not carry a formal budget impact analysis, but considering that the annual costs for PhTx is about 20 times lower than that of WVTT in Canada, and the high prevalence of BPH in men over 60 years of age, we expect that the potential impact might be substantial on healthcare budget, if WVTT were introduced as a first line option.

CONCLUSIONS

WVTT appears to be a cost-effective procedure in the Canadian clinical context, and may be considered as an appropriate first-line alternative to PhTx for patients with moderate-to-severe BPH (with prostate volume less than 80 cm^3) who seek faster improvement, and no lifelong commitment to daily medications.

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Conflicts of interest:

Dean Elterman: Consultant/investigator for Boston Scientific, Olympus, Procept, Prodeon, Urotronic, Zenflow

Naeem Bhojani: Consultant/investigator for Boston Scientific, Olympus, Procept

Bilal Chughtai: Consultant/investigator for Boston Scientific, Olympus, Procept, Prodeon, Urotronic, Zenflow

Kevin C. Zorn: Consultant/investigator for Boston Scientific, Procept

Sahakyan Y, Erman A, Sander B: no conflicts

Figure and Tables

Figure 1. Model structure. The figure was adopted and modified from Chughtai et al (2021).[34] AEs: adverse events; AUR: acute urinary retention, BPH: benign prostate hyperplasia, BT: blood transfusion, Ej.D: ejaculatory dysfunction, Encrust.impl: encrusted implants; Er.D: erectile dysfunction, GM: gynecomastia, Incont: incontinence, IPSS: International Prostate Symptom Score; PhTx: pharmacotherapy; PUL: prostatic urethral lift; TUR: transurethral resection syndrome; TURP: transurethral resection of the prostate; UTI: urinary tract infection; WVTT: water vapor thermal therapy.

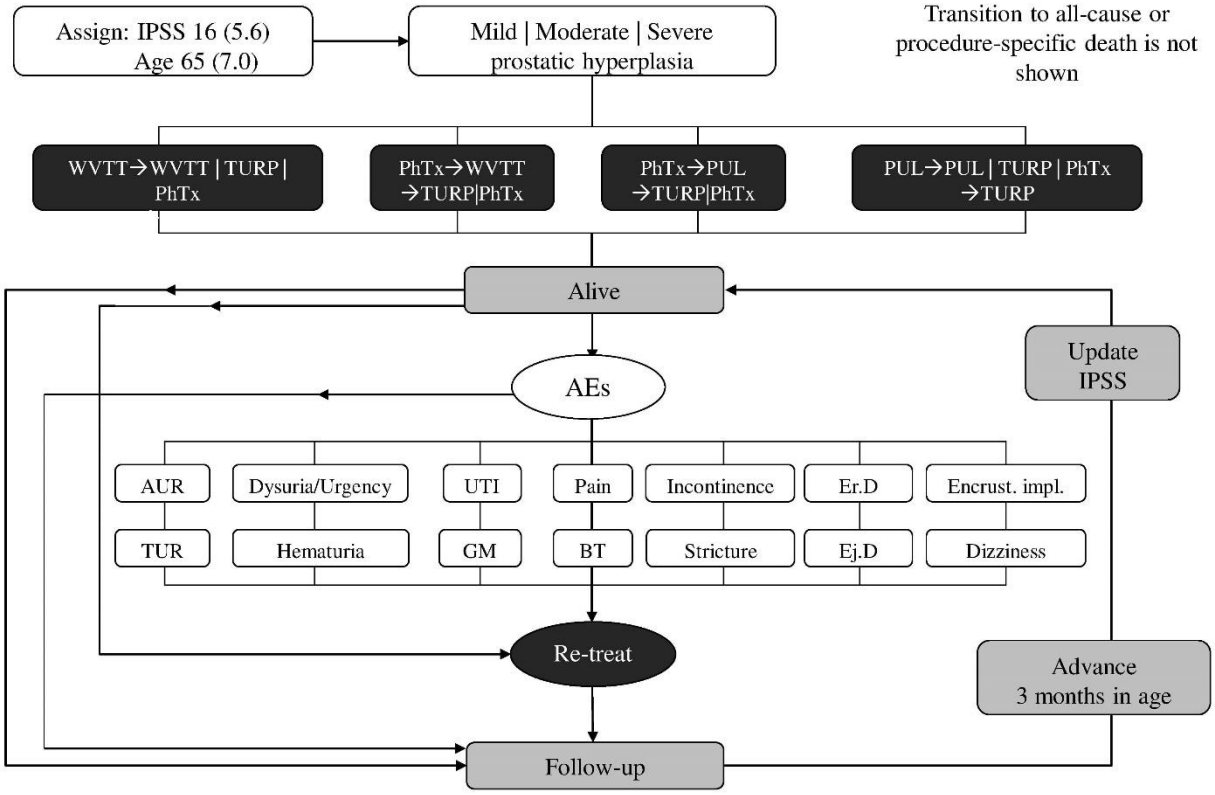

Figure 2. Cost-effectiveness acceptability curve. The graph shows percent of iterations (Y-axis) deemed cost-effective across a range of cost-effectiveness thresholds (X-axis). PhTx: pharmacotherapy; PUL: prostatic urethral lift; WVTT: water vapor thermal therapy

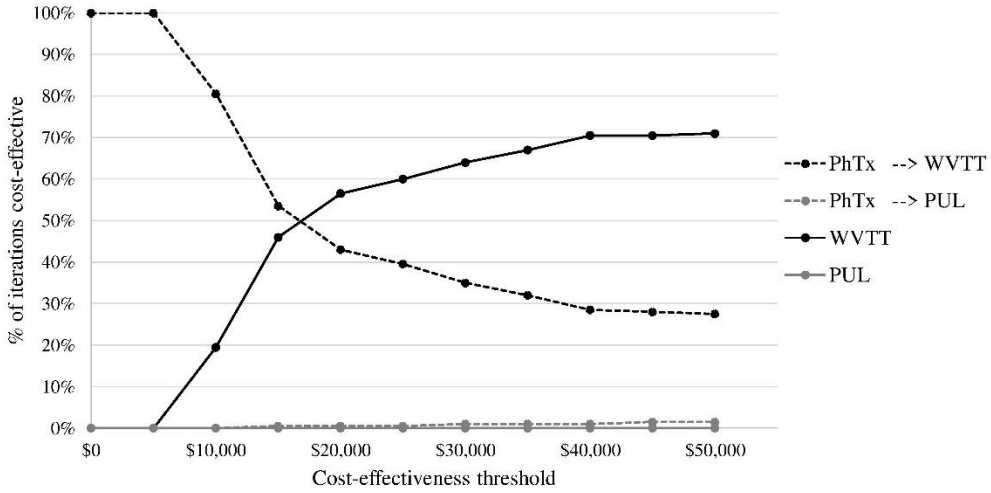

Figure 3. Probabilistic analysis. The graph shows the incremental costs (Y-axis) and incremental QALYs (X-axis) between upfront WVTT vs. pharmacotherapy followed by WVTT for 250,000 simulated individuals and 200 randomly drawn simulations of parameter values; Diagonal dashed line is the $50,000 cost-effectiveness threshold, below which interventions are deemed cost-effective at the set threshold. Dots represent 200 simulations. The grey circle is the 95% credibility interval, i.e. where 95% of simulations lies. Grey dots correspond to simulations where the intervention is considered cost-effective versus comparator and black dots correspond to simulations where the intervention is not cost-effective. E.g., WVTT is considered cost-effective in 73% of simulations (145 out of 200) compared to pharmacotherapy followed by WVTT. PhTx: pharmacotherapy; PUL: prostatic urethral lift; WVTT: water vapor thermal therapy

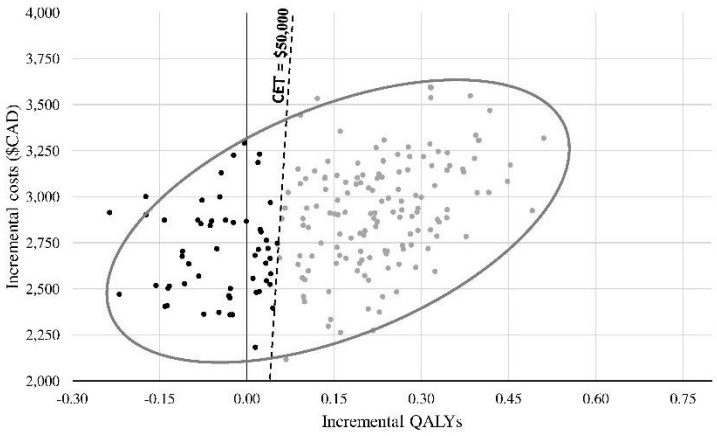

Table 1. Model key parameters			
Parameters	**Mean (SD)**	**Distribution**	**Source**
Age, baseline (years)	65 (7.00)	Normal	9, 11, 15
IPSS, baseline (points)	16.6 (6.35)	Normal	15
Effect of interventions on IPSS			
3-monthly change in IPSS while on PhTx	-0.46 (0.49)	Normal	15
3-monthly change in IPSS while off PhTx	0.11 (0.24)	Normal	20
Change in IPSS after TURP *vs*. baseline score (multiplicative)	0.21 (0.17)	Beta	Calibrated
Mean difference in IPSS after WVTT vs. TURP	4.2 (1.03)	Normal	22
Mean difference in IPSS after PUL vs. TURP	6.3 (0.87)	Normal	22
Effect duration for TURP (years)	7 (5–8)	Triangle	18, 19
Effect duration for WVTT (years)	2 (1–5)	Triangle	Calibrated
Effect duration for PUL (years)	4 (2–5)	Triangle	Calibrated
Cost of interventions			
Cost of WVTT (per procedure)	$5233 (339)	Gamma	29 Supplementary Table 3
Cost of PUL (per procedure)	$8133 (1756)	Gamma	11, 29 Supplementary Table 3
Cost of TURP (per procedure)	$5321 (142)	Gamma	29 Supplementary Table 3
Cost of combination therapy (per 3 months)	$56 (8)	Gamma	27 Supplementary Table 3
Cost of BPH management (per 3 months)	$108 (15)	Gamma	28, 37 Supplementary Table 3

Note: Baseline values and the intervention effects for each simulated patient were randomly sampled from their respective distributions at the start of the model run. The minimum value for baseline age was 40 years and the baseline IPSS score was limited to the range of 8–35 points.
BPH: benign prostatic hyperplasia; IPSS: International Prostate Symptom Score; PhTx: pharmacotherapy; PUL: prostatic urethral lift; SD: standard deviation; TURP: transurethral resection of the prostate; WVTT: water vapor thermal therapy.

Table 2. Discounted (1.5%) lifetime costs (in 2020 $CAD) and QALYs per patient and cost-effectiveness analysis					
Strategy	**Costs**	**QALYs**	**Incremental costs**	**Incremental QALYs**	**ICUR**
All strategies					
PhTx→WVTT→TURP or PhTx	$11 795	15.35	–	–	–
PhTx→PUL→TURP or PhTx	$13 582	15.29	$1787	-0.06	Dominated
WVTT→repeat WVTT or PhTx or TURP→TURP	$14 626	15.50	$1044	0.21	–
PUL→repeat PUL or PhTx or TURP→TURP	$19 151	15.29	$4525	-0.21	Dominated
Dominated strategies were excluded					
PhTx→WVTT→TURP or PhTx	$11 795	15.35	–	–	–
WVTT→repeat WVTT or PhTx or TURP→TURP	$14 626	15.50	$2831	0.15	$18 873

CAD: Canadian dollars; ICUR: incremental cost-utility ratio; PhTx: pharmacotherapy; PUL: prostatic urethral lift; QALYs: quality adjusted life years; TURP: transurethral resection of the prostate; WVTT: water vapor thermal therapy. Note: Strategies are listed by increasing costs. Incremental costs and QALYs were computed relative to the previous less costly strategy.

Table 3. Cost breakdown for the base-case scenario					
All strategies	**Cost of initial treatment**	**Cost of re-treatment**	**AE management**	**BPH management**	**Total**
PhTx→WVTT→TURP or PhTx	$1701	$2706	$286	$7102	$11 795
PhTx→PUL→TURP or PhTx	$1701	$4347	$435	$7099	$13 582
WVTT→repeat WVTT or PhTx or TURP→TURP	$5233	$1921	$371	$7101	$14 626
PUL→repeat PUL or PhTx or TURP→TURP	$8133	$3152	$768	$7098	$19 151

AE: adverse events; BPH: benign prostatic hyperplasia; PhTx: pharmacotherapy; PUL: prostatic urethral lift; TURP: transurethral resection of the prostate; WVTT: water vapor thermal therapy.