Ontario Health

ONTARIO HEALTH TECHNOLOGY ASSESSMENT SERIES

Prostatic Artery Embolization for Benign Prostatic Hyperplasia: A Health Technology Assessment

Key Messages

What Is This Health Technology Assessment About?

Benign prostatic hyperplasia (BPH) is a noncancerous enlargement of the prostate that commonly affects older people. An enlarged prostate can obstruct the flow of urine, which may cause a frequent and urgent need to urinate, incomplete bladder emptying, and loss of bladder control. Symptoms of BPH may initially be mild, but they tend to worsen over time.

Mild to moderate symptoms of BPH are often managed through lifestyle changes and medication. People with moderate to severe symptoms may require minimally invasive or surgical treatment to remove the excess prostate tissue. Prostatic artery embolization (PAE) is an endovascular (within the blood vessel) procedure to treat BPH, in which an interventional radiologist uses a catheter (a thin tube) to insert tiny particles into the body to block blood flow in the prostatic arteries to the enlarged prostate, leading to prostate tissue shrinkage and symptom relief.

This health technology assessment looked at how safe, effective, and cost-effective PAE is compared with other treatment options for people with BPH. It also looked at the budget impact of publicly funding PAE and at the experiences, preferences, and values of people with BPH.

What Did This Health Technology Assessment Find?

We found a limited number of studies comparing PAE with two other procedures for BPH, transurethral resection of the prostate (TURP) and open simple prostatectomy (OSP). We found no high-quality comparative evidence for PAE. Most studies did not have long-term results beyond 1 year, and they included only a small number of study participants. Compared with TURP, PAE may improve BPH symptoms and urodynamic measures, but we are uncertain if the procedure results in similar outcomes. Based on one observational study comparing PAE to OSP, PAE may result in smaller improvements in BPH symptoms and urodynamic measures, but we are very uncertain of the evidence. Compared with TURP and OSP, PAE may result in fewer adverse events.

The economic evidence on PAE is limited. We did not identify any cost-effectiveness studies comparing PAE with alternative treatments for BPH. We did, however, identify three costing studies (including one in Ontario) that showed PAE to be less costly than TURP from the hospital perspective. Based on our primary economic evaluation, PAE is unlikely to be cost-effective. Publicly funding PAE in people with BPH would lead to an additional cost of $11,400 over the next 5 years.

People we spoke with who had lived experience with BPH reported significant disruptions of their quality of life, including in relationships and employment. Many of them had experience with PAE and reported a positive experience with the procedure and meaningful improvement in their lives, despite knowing that the benefits may not be permanent.

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The statements, conclusions, and views expressed in this report do not necessarily represent the views of those we consulted.

A Note About Terminology

As a government agency, Ontario Health can play an active role in ensuring that people of all identities and expressions recognize themselves in what they read and hear from us. We recognize that gender identities are individual and that some people who have a prostate do not identify as men, despite being assigned male sex at birth. Thus, in this health technology assessment, we use gender-inclusive pronouns and terms as much as possible. However, when citing published literature that uses the terms "man," "men," or "male," we also use these terms for consistency with these cited studies.

Citation

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Abstract

Background

Benign prostatic hyperplasia (BPH) is a noncancerous enlargement of the prostate that commonly affects older people with prostates and may lead to obstructive urinary symptoms. Symptoms may initially be mild but tend to worsen over time. Prostatic artery embolization (PAE) is an endovascular procedure to treat BPH, wherein an interventional radiologist inserts a catheter into the patient to inject tiny particles intended to reduce blood flow to the enlarged prostate, causing it to shrink in size. We conducted a health technology assessment on PAE for people with BPH, which included an evaluation of effectiveness, safety, cost-effectiveness, the budget impact of publicly funding PAE, and patient preferences and values.

Methods

We performed a systematic literature search of the clinical evidence. We assessed the risk of bias of each included study using the Cochrane Risk of Bias tool for randomized controlled trials (RCTs) and the Risk of Bias in Nonrandomized Studies—of Interventions (ROBINS-I) tool for observational studies. We assessed the quality of the body of evidence according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group criteria. We performed a systematic review of the economic literature. We then assessed the cost-effectiveness of PAE compared with alternative treatments (i.e., transurethral resection of the prostate [TURP] or open simple prostatectomy [OSP]) using a Markov microsimulation model. The analysis was conducted from the Ontario Ministry of Health perspective over a time horizon of 6.5 years. We also analyzed the budget impact of publicly funding PAE in people with moderate to severe BPH in Ontario.

Results

We included six studies in our systematic review. Four RCTs and one observational study compared PAE with TURP, and one observational study compared PAE with OSP. All studies had considerable risk-of-bias concerns. PAE may improve BPH symptoms and urodynamic measures, but we are uncertain whether PAE achieves better results than TURP (GRADE: Very low to Low). Compared with TURP, PAE may result in higher patient satisfaction and fewer adverse events (GRADE: Not assessed). Compared with OSP, PAE may result in smaller improvements in BPH symptoms and urodynamic measures and may lead to fewer adverse events, but the evidence is very uncertain (GRADE: Very low).

We did not find any published cost-effectiveness studies in the economic literature review. Our primary economic evaluation showed that, compared with TURP, PAE has an incremental cost of $328 (95% CrI: −$686 to $1,423) and a very small incremental quality-adjusted life-year (QALY) of 0.007 (95% CrI: −0.004 to 0.018). The resulting incremental cost-effectiveness ratio (ICER) of PAE versus TURP is $44,930 per QALY gained. At the commonly used willingness-to-pay values of $50,000 and $100,000 per QALY, the cost-effectiveness of PAE is uncertain (52% and 68% probability, respectively, of being cost-effective compared with TURP). In a scenario analysis, we compared PAE with OSP for individuals with large prostates (who may be ineligible for TURP). We found that PAE is less costly (−$1,231; 95% CrI: −$2,457 to $69) and less effective (−0.12 QALYs; 95% CrI: −0.18 to −0.04). The resulting ICER of PAE versus OSP is $10,241 saved per QALY lost. At the commonly used willingness-to-pay value of $50,000 per QALY, PAE is unlikely to be cost-effective (2% probability of being cost-effective compared with OSP). Assuming a low uptake (i.e., an additional 10 to 50 procedures per year in years 1 to 5), we estimated that publicly funding PAE in Ontario would lead to an additional cost of about $11,400 over the next 5 years.

People we spoke with who have lived experience with BPH reported on the negative impact it can have on their quality of life. Those who had received PAE reported a positive experience with the procedure and meaningful improvement in their symptoms.

Conclusions

Prostatic artery embolization may improve BPH symptoms and urodynamic measures, but we are uncertain if the procedure results in similar outcomes to those of TURP. Based on one observational study, PAE may result in smaller improvements compared with OSP, but we are very uncertain of the evidence. Compared with TURP and OSP, PAE may result in fewer adverse events. Longer-term comparative studies are needed to assess the durability and long-term adverse events of PAE, the potential need for reintervention after PAE, and how PAE compares with other available BPH treatment options.

We found the cost-effectiveness of PAE compared with TURP to be uncertain. Also, PAE is unlikely to be cost-effective compared with OSP. If PAE is publicly funded in Ontario, the budget impact is estimated to be small over the next 5 years.

People who have lived experience with BPH reported that PAE improves quality of life and reduces negative symptoms of BPH.

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Objective

This health technology assessment evaluates the effectiveness, safety, and cost-effectiveness of prostatic artery embolization (PAE) for people with benign prostatic hyperplasia (BPH). It also evaluates the budget impact of publicly funding PAE and the experiences, preferences, and values of people with BPH.

Background

Health Condition

The prostate gland produces the fluid that carries sperm. Benign prostatic hyperplasia is a condition in which a person has an enlargement of the prostate gland caused by an overgrowth of cells in the transition zone of the prostate (the area surrounding the urethra). Symptoms of BPH include weak or slow urine stream, frequent urination, nocturia (frequent nighttime urination), urgency, straining, inability to completely empty the bladder, and incontinence. Benign prostatic hyperplasia is a noncancerous (benign) condition and does not increase the risk of prostate cancer.[1] Risk factors for BPH include age, family history, obesity, heart disease, and diabetes.[1]

There are different types of tests to diagnose BPH and help rule out other possible health conditions, including a physical exam, digital rectal exam, urinalysis, blood tests (to measure increased prostate-specific antigen [PSA] levels), urodynamic tests (to assess how well the bladder and urethra hold and release urine), transrectal ultrasound (to determine prostate volume), cystoscopy (a procedure to view the inside of the bladder or urethra), and biopsy.

Common urodynamic tests include uroflowmetry and the post-void residual volume test. Uroflowmetry assesses urine flow using an electronic uroflowmeter (a device that measures urine flow) connected to a funnel for urine collection. The flow rate (the amount of urine that passes per second) is calculated, and the peak or maximum flow rate (Q_{max}) can determine the severity of urine obstruction (i.e., the severity of the BPH). In general, a peak urinary flow rate greater than 15 mL/s to 20 mL/s is considered normal for people with prostates. Post-void residual volume (the amount of urine retained in the bladder after voluntary bladder emptying) is measured either by draining the bladder with a catheter or by ultrasound. Volumes less than 50 mL to 100 mL are generally considered normal.

The severity of symptoms in people with BPH varies and tends to gradually worsen over time. Prostate size does not necessarily determine symptom severity. Symptoms are commonly referred to collectively as lower urinary tract symptoms (LUTS), secondary to BPH. In severe cases, complications of BPH include urinary tract infection, acute urinary retention (inability to urinate), hematuria (blood in the urine), bladder stones, and kidney damage.

The International Prostate Symptom Score (IPSS) is a validated questionnaire used to assess the symptoms of BPH. The tool consists of seven questions that assess bladder emptying, urination frequency, intermittency, urgency, stream, and strain, and nocturia.[2] Symptom scores are categorized as mild (≤ 7), moderate (8–19), and severe (20–35). The IPSS tool also contains a question that assesses a person's quality of life due to their urinary symptoms (IPSS—Quality of Life), with scores ranging from 0 ("delighted") to 6 ("terrible").[2]

Clinical Need and Target Population

The prevalence of BPH increases after 40 years of age.[3] It has been estimated that 50% of people over 75 years of age who have a prostate have lower urinary tract symptoms due to BPH. While BPH is not typically a life-threatening condition, its symptoms can significantly impact a person's quality of life.

Current Treatment Options

Treatment for BPH is necessary only if symptoms become bothersome. Mild symptoms are usually managed conservatively, such as with lifestyle changes (e.g., exercise, dietary modifications), bladder training, or pelvic floor exercises.[1]

Treatment options for BPH include medications and surgical or minimally invasive procedures. Symptom severity, prostate volume, age, health, and comorbid conditions are considered when determining treatment. Medications are typically the first-line treatment and may include alpha-blockers (to relax the bladder neck muscles and muscle fibres in the prostate for easier urination), 5-alpha-reductase inhibitors (to block hormones that promote prostate gland growth), muscle relaxants, or combination therapy. Catheterization, in which a catheter is inserted through the penis to drain urine from the bladder into a drainage pouch, may be used in cases of acute urinary retention secondary to BPH. If BPH symptoms worsen, minimally invasive or surgical procedures may be considered to remove the excess tissue or shrink the prostate gland. These procedures may cause complications such as urinary incontinence, urinary urgency, infection, bleeding, and, in rare cases, ejaculation disorders or erectile dysfunction. Surgical and minimally invasive procedures for BPH include the following.

Surgical Procedures

- Transurethral resection of the prostate (TURP), in which excess tissue is removed using a resectoscope (a thin, tube-like instrument for removing tissue from inside the body) inserted through the penis
- Transurethral incision of the prostate (TUIP), in which incisions are made in the bladder neck and the prostate to widen the urethra
- Laser surgery, in which a laser is passed through a scope to remove excess tissue; for example, holmium laser ablation of the prostate (HoLAP), holmium laser enucleation of the prostate (HoLEP), thulium laser enucleation of the prostate (ThuLEP), and photoselective vaporization (PVP)
- Transurethral electrovaporization (TUVP), in which an electrode heats and destroys the excess tissue
- Transurethral water-jet ablation (aquablation), in which a high-speed jet of water destroys the excess tissue
- Simple prostatectomy, in which excess tissue is removed through incisions typically made in the lower abdomen (can also be performed laparoscopically or in a robot-assisted approach)

Minimally Invasive Procedures

- Transurethral microwave thermotherapy (TUMT), in which a small microwave antenna emits microwave energy that heats and destroys the excess tissue
- Transurethral water vapour thermotherapy, in which targeted and controlled water vapour is injected to destroy the excess tissue
- Transurethral needle ablation (TUNA), in which radio waves passed through needles generate heat and destroy the excess tissue
- Prostatic urethral lift (PUL), in which implants are placed to pull the prostate away from the urethra

Endovascular Procedure

- Prostatic artery embolization (PAE), in which tiny particles are inserted through a catheter in the prostatic arteries to reduce the blood supply to the prostate gland

Transurethral resection of the prostate is the standard procedure to treat BPH, but it requires general anesthesia and hospitalization. The procedure typically takes less than 60 minutes and can be performed through a monopolar or a bipolar approach. Monopolar TURP is the conventional approach and uses an electrical current that passes through an active electrode (connected to the resectoscope) to the patient. Risks include skin burns, nerve damage, and inadvertent nerve stimulation. In addition, monopolar TURP uses a non-conducting hypo-osmolar irrigation fluid (e.g., glycine) that can cause dilutional hyponatremia (low sodium concentration in the blood) and, in rare cases, transurethral resection (TUR) syndrome (if severe, it may cause convulsions, coma, or even death). Bipolar TURP was developed to address the disadvantages of monopolar TURP. It uses electricity cycling between active and passive electrodes to release energy locally to the tissue on contact. This causes tissue vaporization and decreases the risk of thermal injury. Normal saline is used in bipolar TURP for irrigation, which eliminates the risk of hyponatremia and TUR syndrome.

In Ontario, photoselective vaporization has been recommended by the Ontario Health Technology Advisory Committee as an effective, safe, and cost-effective alternative to TURP[4] and may benefit frail and anticoagulated people in particular. Open simple prostatectomy (OSP) is not commonly performed in Ontario or other provinces in Canada for BPH and is typically reserved for people with very large prostates (> 100 mL prostate volume; Dean Elterman, MD, telephone communication, September 24, 2019). Among Canadian urology training centres in 2018, the mean number of OSPs per academic training program was only 4.7 cases annually.[5] Most centres performing simple prostatectomy in Canada and globally are being performed with robot-assisted surgery (Kevin Zorn, MD, written communication, July 15, 2020). Transurethral needle ablation is not recommended by the Canadian Urological Association for BPH.[6] Other office-based minimally invasive procedures, including transurethral water vapour thermotherapy (treatment time < 10 min) and prostatic urethral lift (treatment time 20–30 min) have Health Canada approval. Transurethral water vapour thermotherapy has the advantage of also treating BPH in people with median lobes.[7]

Health Technology Under Review

First performed in 2009, PAE begins with the insertion of a catheter via the right or left femoral artery (in the groin) or radial artery (in the wrist) under x-ray guidance. Very selective catheterization is

achieved using fine microcatheters in the pelvic arteries that lead to the prostate gland. In a process known as arteriography, a contrast medium (x-ray dye) is injected through the catheter to map the blood flow of the small arteries that supply the prostate gland. Embolic particles are then injected through the catheter to achieve embolization, forming clots in the prostatic arteries that block the prostate gland's blood supply, causing it to undergo necrosis (localized cell death). Symptoms resolve in the following days and weeks after the procedure as the enlarged prostate gland gradually reduces in size.

Embolic particles used vary by material (e.g., polyvinyl alcohol or trisacryl with gelatin), shape (spherical or irregular), and size (50–300 μm). Some embolic particles are biodegradable, whereas others are not and thus remain in the occluded arteries. The type and size of embolic particle may impact clinical outcomes.[8-11] Different PAE approaches are also possible: unilateral or bilateral embolization (one or both sides of the prostate gland, respectively), the use of a single type of embolic particle, or a combination of different-sized particles. Embolization can also be performed proximally first, and then distally (known as Proximal Embolization First Then Distal Embolization, or the PErFecTED technique).[12] For the PErFecTED approach, the proximal urethral group of arteries is embolized first, then distal embolization completes occlusion of blood flow to the prostate gland. According to Carnevale et al,[12] this technique allows better distribution of embolic particles in the intraprostatic arteries and reduces risk of spasm or blood clots.

The reported procedure time for PAE ranges between 90 and 150 minutes[13-17] and is performed in a specialized angiography unit by an interventional radiologist. It is a day procedure using local anesthesia. Unlike other more invasive surgical options for BPH, general anesthesia and hospitalization are generally not required. Reported procedure times for PAE done under sedation range from 2 to 4 hours (Kevin Zorn, MD, written communication, July 15, 2020). Compared with TURP—the standard procedure for BPH—patients may prefer the less invasive nature and faster recovery time of PAE.

Technical and clinical failures can occur. Cases of technical failure are primarily related to intra-procedural evidence of highly tortuous (curved or twisted) arteries or occluded arteries. In this case, TURP or other surgical management may be pursued instead of PAE. Studies typically report technical success rates greater than 90% for PAE.[18] Bilateral embolization is the optimal outcome for PAE; however, in some cases, only unilateral embolization is technically possible.

Clinical success occurs when the patient's symptoms improve. It is possible for patients who have achieved clinical success from any treatment to regress over time and require surgical intervention or medical reinitialization for BPH.

Prostatic artery embolization is a technically demanding endovascular radiographic procedure that is generally safe, but adverse effects and complications may occur. Serious complications occur in less than 5% of people.[19] In the first days after the procedure, people may experience post-PAE pain syndrome from tissue ischemia. Symptoms may include nausea, vomiting, pelvic pain, or frequent urination. Other complications from PAE may include bleeding, hematuria (blood in the urine), hematospermia (blood in the semen), urinary retention, ejaculation disorders (e.g., decrease in ejaculation volume), urinary infection, or urethral or bladder neck stricture (narrowing of the urethra or bladder neck). Access site hematoma and pseudoaneurysm formation have also been reported. The contrast materials used during PAE are nephrotoxic (toxic to the kidneys).

Since PAE involves an arteriogram, radiation exposure from x-rays may also be a concern for people, especially those of a younger age, when considering the possible accumulation of exposure over a lifetime. It has been estimated that the radiation exposure from PAE is comparable to other complex interventional exposures[20]; however, the long-term impact of radiation exposure from PAE has not been well studied.

Regulatory Information

Embolic particles for prostatic artery embolization are regulated by Health Canada as Class IV medical devices. Embosphere Microspheres (licence number 65176) from Merit Medical and Occlusin Embolization Microspheres (Ekobi 500, licence number 101802) from IMBiotechnologies have Health Canada approval for BPH. The U.S. Food and Drug Administration (FDA) has approved Embosphere Microspheres from Merit Medical and Embozene Microspheres from Varian for BPH.

Guidelines

Multiple Canadian and international guidelines have been published on PAE; these are summarized in Appendix 1. The 2018 Canadian Urological Association guideline does not recommend PAE for the treatment of lower urinary tract symptoms associated with BPH (conditional recommendation based on moderate-quality evidence).[6] The Canadian Urological Association does not recommend this approach for the management of BPH for the typical patient because of the inferior urodynamic improvements and larger adverse events when compared to TURP and OSP, and the greater urinary retention rates after the procedure (Kevin Zorn, MD, written communication, July 15, 2020). The American Urological Association also does not recommend PAE for lower urinary tract symptoms for BPH outside the context of a clinical trial, based on expert opinion.[21]

In contrast, the Society of Interventional Radiology (SIR) multi-society consensus position statement (endorsed by the Canadian Association for Interventional Radiology) recommends PAE as an acceptable minimally invasive treatment option for appropriately selected people with BPH with moderate to severe lower urinary tract symptoms (strong recommendation).[22] The German Society for Interventional Radiology published a position paper on PAE, which notes that the procedure is a patient-friendly, minimally invasive, alternative therapy option for BPH.[23] In the United Kingdom, the National Institute for Health and Care Excellence guidance noted that the current evidence on the safety and efficacy of PAE was adequate to support its use, provided that standard arrangements are in place for clinical governance, consent, and audit.[24] The European Association of Urology recommends offering PAE to people with moderate to severe lower urinary tract symptoms who wish to consider minimally invasive treatment options and are willing to accept less optimal objective outcomes compared with TURP (weak recommendation).[25] The guideline also recommends that PAE be performed only in units where work up and follow up are performed by urologists working collaboratively with trained interventional radiologists to identify people suitable for PAE (strong recommendation).

The Cardiovascular and Interventional Radiological Society of Europe has also published guidance on standards of practice for PAE[26] and the Society of Interventional Radiologists has guidance on research reporting standards for PAE.[27]

In July 2020, the FDA published draft guidance for the investigation of devices used in the treatment of BPH for industry and FDA administration staff.[28] While the draft guidance does not specifically include PAE, the FDA proposed that embolic particles for BPH treatment be added in the scope of the final guidance document. The draft guidance contains nonbinding recommendations on non-clinical testing

(e.g., animal studies), pilot studies, randomization and controls, study endpoints (primary effectiveness endpoint, primary safety endpoint, and secondary endpoints), statistical hypotheses, patient selection criteria, post-treatment evaluations, and statistical analyses (for primary and secondary endpoint analyses and missing data).

Ontario and Canadian Context

In Ontario, PAE is currently performed at only one hospital, which also performs the largest volume of PAE procedures in Canada (Kong Teng Tan, MD, telephone communication, September 20, 2019). Procedures were first performed in 2016, and annual volumes have been fairly stable because the number of PAE procedures are limited (Kong Teng Tan, MD, telephone communication, September 20, 2019). About 40 PAE procedures are performed per year (about once per week). Potential candidates for PAE must be referred to an interventional radiologist by a urologist for PAE (Dean Elterman, MD, telephone communication, September 24, 2019). Polyvinyl alcohol embolic particles are used at the hospital for PAE (Kong Teng Tan, MD, written communication, February 4, 2020). Based on a retrospective study at the hospital, PAE resulted in a clinically and statistically significant reduction in prostate volume and improvement in BPH symptoms, quality of life, and urodynamic measures at one year.[29]

There is no specific Ontario Health Insurance Plan (OHIP) fee code for PAE. Fee codes for professional fees cover general catheterization and embolization (about $680 CAD per procedure), but there is no specific public funding for embolic particles.[30] Embolic particles are paid for through the hospital global budget (Kong Teng Tan, MD, telephone communication, September 20, 2019). Based on an Ontario costing study,[31] the estimated cost of PAE per patient, excluding professional fees, was about $5,200. Costs were mainly related to the angiography unit, consumables, and the recovery room.

Prostatic artery embolization is also performed at academic hospitals in Vancouver, Edmonton, and Montreal (Kong Teng Tan, MD, telephone communication, September 20, 2019). The volumes for PAE at these centres are lower than in Ontario (< 10 cases per year), and there is no specific public funding for PAE in other provinces (Kong Teng Tan, MD, telephone communication, September 20, 2019).

Systematic Reviews

Numerous systematic reviews have been conducted on PAE in recent years (see Appendix 2 for a summary). These systematic reviews differed slightly in their comparators, outcomes of interest, method of analysis, and study eligibility criteria compared with our research question. We used these reviews as a reference source for relevant studies that may meet our inclusion criteria.

Expert Consultation

We engaged with experts in the specialty areas of interventional radiology, urology, family medicine, and health economics to help inform our understanding of aspects of the health technology and our methodologies and to contextualize the evidence.

PROSPERO Registration

This health technology assessment has been registered in PROSPERO, the international prospective register of systematic reviews (CRD 42020160883), available at https://www.crd.york.ac.uk/PROSPERO.

Clinical Evidence

Research Question

What are the effectiveness and safety of prostatic artery embolization (PAE) compared with surgical and minimally invasive procedures for the treatment of people with benign prostatic hyperplasia (BPH)?

Methods

Clinical Literature Search

We performed a clinical literature search on November 7, 2019, to retrieve studies published from inception until the search date. We used the Ovid interface in the following databases: MEDLINE, Embase, the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, the Health Technology Assessment database, and the National Health Service Economic Evaluation Database (NHS EED).

A medical librarian developed the search strategies using controlled vocabulary (e.g., Medical Subject Headings) and relevant keywords. The final search strategy was peer-reviewed using the PRESS Checklist.[32]

We created database auto-alerts in MEDLINE and Embase and monitored them until the end of May 2020. We also performed a targeted grey literature search of health technology assessment agency websites as well as clinical trial and systematic review registries. The grey literature search was updated on August 14, 2020. See Appendix 3 for our literature search strategies, including all search terms.

Eligibility Criteria

STUDIES

Inclusion Criteria

- English-language full-text publications
- Studies published from database inception until November 7, 2019
- Systematic reviews, randomized controlled trials (RCTs), prospective comparative nonrandomized studies

Exclusion Criteria

- Non-systematic reviews, narrative reviews, noncomparative studies, retrospective studies, abstracts, editorials, letters, case reports, and commentaries
- Animal and in vitro studies

PARTICIPANTS

- People with BPH, any age or severity

INTERVENTIONS

- PAE using any type and size of embolic particles

- PAE via the femoral or radial artery using any embolization approach
- Comparator: any surgical or minimally invasive procedure for BPH

OUTCOME MEASURES

- International Prostate Symptom Score (IPSS)
- Health-related quality of life
- Erectile function
- Peak (maximum) urinary flow rate
- Post-void residual urine volume
- Prostate volume
- Prostate-specific antigen (PSA) level
- Clinical success
- Patient satisfaction
- Adverse events (e.g., non-target embolization, hematuria, hematospermia, urinary infection, urinary retention, urinary incontinence, or urethral or bladder neck stricture)

Literature Screening

A single reviewer conducted an initial screening of titles and abstracts using Covidence[33] and then obtained the full texts of studies that appeared eligible for review according to the inclusion criteria. A single reviewer then examined the full-text articles and selected studies eligible for inclusion. The reviewer also examined reference lists.

Data Extraction

A single reviewer extracted relevant data on study characteristics and risk-of-bias items using a data form to collect information on the following:

- Source (e.g., citation information, study type)
- Methods (e.g., study design, study duration and years, participant allocation, allocation sequence concealment, blinding, reporting of missing data, reporting of outcomes, whether the study compared two or more groups)
- Outcomes (e.g., outcomes measured, number of participants for each outcome, number of participants missing for each outcome, outcome definition and source of information, unit of measurement, upper and lower limits [for scales], time points at which the outcomes were assessed)

We contacted study authors to provide clarification as needed.

Statistical Analysis

Meta-analysis was not conducted due to clinical and statistical heterogeneity. The results were instead summarized narratively and in tabular form.

For studies that presented 95% confidence intervals in graphical form only, we used WebPlotDigitizer[34] to extract estimated values from the graphs. Mean changes from baseline and their associated standard deviations were imputed if they were not reported in the studies, assuming a positive correlation of one between the baseline and follow-up measurement. We used the following formula to impute these standard deviations: $SD_{\text{change from baseline}} = \sqrt{SD^2_{\text{baseline}} + SD^2_{\text{follow-up}}}$.[35]

Critical Appraisal of Evidence

We assessed the risk of bias using the Cochrane Risk of Bias tool[36] for RCTs and the Risk of Bias in Non-randomized Studies—of Interventions (ROBINS–I) tool[37] for observational studies (Appendix 4).

We evaluated the quality of the body of evidence for each outcome according to the *Grading of Recommendations Assessment, Development, and Evaluation* (GRADE) *Handbook*.[38] The body of evidence was assessed based on the following considerations: risk of bias, inconsistency, indirectness, imprecision, and publication bias. The overall rating reflects our certainty in the evidence.

Results

Clinical Literature Search

The database search of the clinical literature yielded 570 citations published from database inception until November 7, 2019. We identified seven additional studies from other sources, for a total of 330 after removing duplicates. Six studies[13-17,39] (four RCTs[13,14,16,39] and two observational studies[15,17]) met our inclusion criteria. One of the included studies (Insausti et al[16]) was found after the search date through MEDLINE auto-alerts. Figure 1 presents the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram for the clinical literature search.

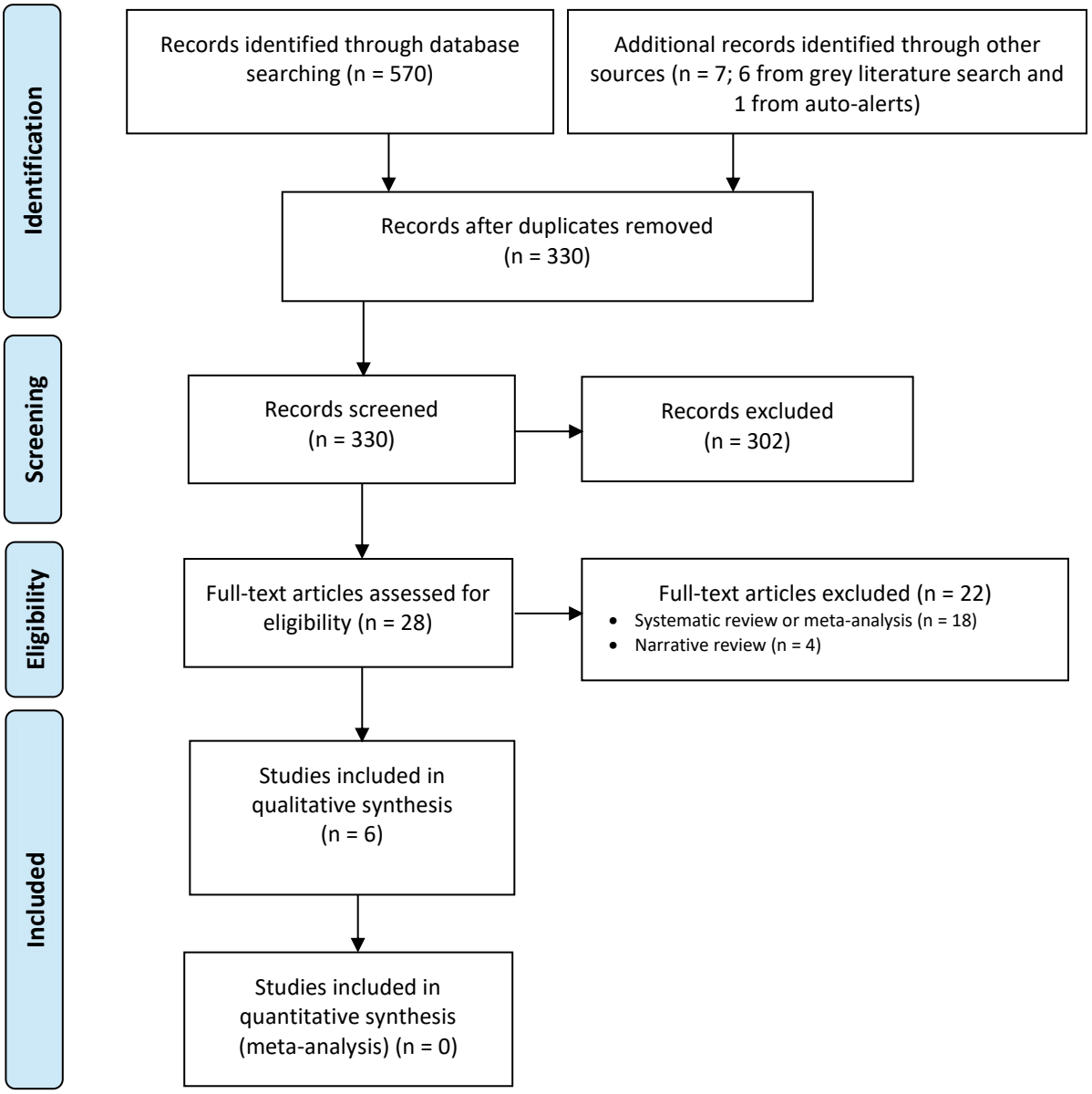

Figure 1: PRISMA Flow Diagram—Clinical Search Strategy

Abbreviation: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses.
Source: Adapted from Moher et al.[40]

Characteristics of Included Studies

Six studies were included in the review, from Brazil, China, Italy and Russia, Spain, Switzerland, and the United Kingdom.[13-15,17,39] Five studies (four RCTs[13,14,16,39] and one nonrandomized study[15]) compared PAE with TURP, and one nonrandomized study[17] compared PAE with open simple prostatectomy (OSP). We found one retrospective study that compared PAE with TURP[41] and another RCT that compared PAE with sham.[42] We excluded these two studies based on our eligibility criteria during the title and abstract study screening stage. We also excluded four RCTs that compared only different types and sizes of embolic particles for PAE.[8-11] Table 1 presents the study characteristics of the six included studies.

Studies on PAE compared with TURP varied in their population inclusion criteria, the type and size of embolic particles used (Embosphere, Embozene, or polyvinyl alcohol embolic particles), and the type of TURP performed (monopolar or bipolar). Prostate volumes were variable among the included patient populations and information on the presence of median lobes was not included. Ray et al[15] combined both monopolar and bipolar TURP as the comparator, noting that the procedures have been shown to provide very similar functional outcomes. Carnevale et al[39] compared both the original PAE approach with their PErFecTED (Proximal Embolization First Then Distal Embolization) technique with TURP. PAE was performed via the transfemoral approach in all studies that specified PAE approach.

The follow-up duration of three of the five included studies was 1 year.[15,17,39] Abt et al[14] compared PAE with TURP, but published only interim 12-week results (from a planned 2-year follow-up). Gao et al[13] had the longest follow-up of the included studies, with 2-year data that compared PAE with TURP.

Table 1: Characteristics of Included Studies

Study Country	Study Design	N	Participants	Mean Age ± SD	PAE Details	Comparator Details	Follow-Up Time	Funding Source
PAE vs. TURP								
Abt et al, 2018[14] Switzerland	Noninferiority RCT	Total: 99 48 PAE 51 TURP	Included: men ≥ 40 y old, indicated for TURP, refractory to medical treatment or not willing to undergo or continue medical treatment, prostate size 25–80 mL, IPSS ≥ 8, IPSS QOL ≥ 3, Q_{max} < 12 mL/s or urinary retention, written informed consent Excluded: severe atherosclerosis, aneurysmatic changes or severe tortuosity in the aortic bifurcation or internal iliac arteries, acontractile detrusor, neurogenic lower urinary tract dysfunction, urethral stenosis, bladder diverticulum, bladder stone, allergy to intravenous contrast media, contraindication for MRI, prostate cancer, renal failure (GFR < 60 mL/min)	PAE: 65.7 ± 9.3 TURP: 66.1 ± 9.8	250–400 µm Embozene microspheres (previously Boston Scientific, now Varian) under local anesthesia via femoral artery	Monopolar TURP under spinal or general anaesthesia	1, 6, 12 wk (interim results)	Research grant from St. Gallen Cantonal Hospital Funder had no role in the conduct or analysis of the trial No conflicts of interests
Carnevale et al, 2016[39] Brazil	RCT	Total: 45 15 original PAE 15 PErFecTED 15 TURP	Included: > 45 years old, IPSS > 19, symptoms refractory to medical treatment for ≥ 6 mo; negative screening for prostate cancer; prostate volume 30–90 cm^3, bladder outlet obstruction Excluded: renal failure, bladder calculi or diverticula, suspected prostate cancer, urethral stenosis, neurogenic bladder disorders	Original PAE: 63.5 ± 8.7 PErFecTED: 60.4 ± 5.2 TURP: 66.4 ± 5.6	300–500 µm Embosphere microspheres (Merit Medical) under local anesthesia via femoral artery Original PAE and PErFecTED technique	Monopolar TURP under spinal anesthesia	12 mo	Funding sources not reported No financial disclosures
Gao et al, 2014[13] China	RCT	Total: 114 57 PAE 57 TURP	Included: IPSS > 7 after failed medical therapy with a washout period ≥ 2 wk, prostate volume 20–100 mL, Q_{max} < 15 mL/s, written informed consent Excluded: detrusor hyperactivity or hypocontractility, urethral stricture, prostate cancer, diabetes mellitus, previous prostate or bladder neck or urethral surgery	PAE: 67.7 ± 8.7 TURP: 66.4 ± 7.8	355–500 µm PVA microspheres (Cook Medical) under local anesthesia via femoral artery (bilateral or unilateral)	Bipolar TURP under epidural anesthesia	1, 3, 6, 12, 24 mo	Funding sources not reported No conflicts of interest reported
Insausti et al, 2020[16] Spain	Noninferiority RCT	Total: 45 23 PAE 22 TURP	Included: > 60 years old, BPH-related LUTS refractory to medical treatment for ≥ 6 mo or could not tolerate medical treatment, TURP was	PAE: 72.4 ± 6.2 TURP: 71.8 ± 5.5	300–500 µm Bead Block PVA microspheres	Bipolar TURP	3, 6, 12 mo	Unrestricted grant from Boston Scientific

Study Country	Study Design	N	Participants	Mean Age ± SD	PAE Details	Comparator Details	Follow-Up Time	Funding Source
			indicated, IPSS ≥ 8, QOL ≥ 3, Q_{max} ≤ 10 mL/s or urinary retention Excluded: advanced atherosclerosis and tortuosity of iliac arteries, nonvisualization of the prostatic artery or other accessory arteries on CT angiography, urethral stenosis, detrusor failure or neurogenic bladder, GFR < 30 mL/min, prostate cancer		(Boston Scientific)			
Ray et al, 2018[15] United Kingdom	Prospective, comparative observational study (noninferiority analysis)	Total: 305 216 PAE 90 TURP	Included: men with LUTS who consented to undergo PAE, TURP, OP, or HoLEP in one of the UK-ROPE collaborating centres, able to read, write, and understand English, written informed consent	PAE: 66 ± 7.4 TURP: 70 ± 7.5	PVA microspheres (Cook Medical)	Monopolar and bipolar TURP	1, 3, 6, 12 mo	Research grant from Cook Medical to fund PAE cases Grants from British Society of Interventional Radiologists and British Association of Urological Surgeons for online register setup
PAE vs. OSP								
Russo et al, 2015[17] Italy, Russia	Prospective, comparative observational study	Total: 160 80 PAE 80 OSP	Included: symptomatic LUTS due to benign prostatic obstruction, IPSS > 12, PSA level < 4 ng/mL or 4–10 ng/mL, but with negative prostate biopsy, prostate volume > 80 cm^3, Q_{max} < 15 mL/s Excluded: neurogenic bladder dysfunction and/or sphincter decompensation, coagulation disorders and/or antiplatelet or anticoagulant therapy, chronic kidney disease, previous surgical treatment for LUTS due to benign prostatic obstruction or therapy with 5-alpha reductase inhibitors, life expectancy < 2 y, current diagnosis of bladder stones, people with catheter or with an episode of acute retention of urine in the last 4 wk	PAE: 67.0 ± 5.72 TURP: 68.4 ± 6.13	300–500 µm Embosphere microspheres (Merit Medical)	Suprapubic transvesical open prostatectomy	1, 6, 12 mo	Funding sources not reported Conflicts of interest not reported

Abbreviations: BPH, benign prostatic hyperplasia; CT, computed tomography; GFR, glomerular filtration rate; HoLEP, holmium laser enucleation of the prostate; IPSS, International Prostate Symptom Score; LUTS, lower urinary tract symptoms; MRI, magnetic resonance imaging; OSP, open simple prostatectomy; PAE, prostatic artery embolization; PErFecTED, proximal embolization first then embolize distal method of prostatic artery embolization; PVA, polyvinyl alcohol; Qmax, peak (maximum) urinary flow rate; QOL, quality of life; RCT, randomized controlled trial; SD, standard deviation; TURP, transurethral resection of the prostate.

Risk of Bias in the Included Studies

All the included RCTs had considerable or serious risk-of-bias concerns (see Appendix 4, Tables A3 and A4). In general, each RCT had a small number of participants, and the authors did not clearly report the method of randomization. Participants and physicians were not blinded, but this likely was not possible due to the differences between the PAE and TURP procedures.

Gao et al[13] randomly assigned participants to PAE or TURP, but participants could refuse the assigned treatment group and be offered other treatment options. Participants refusing their group assignment were excluded from the analysis. These participants may have differed from those included in the study (no information was provided on the characteristics of excluded participants). Similarly, Insausti et al[16] excluded patients who did not receive the allocated treatment or who discontinued the intervention.

In the study by Gao et al,[13] TURP was repeated 6 months after the initial procedure in the case of clinical failure. Results for participants who underwent repeat procedures were included in the analysis when available, but results after the repeat procedure were excluded. The authors also reported different numbers of participants analyzed for "early" and "late" follow-up time periods, but the duration of these periods was unclear.

Carnevale et al[39] compared both the original PAE approach and their PErFecTED technique with TURP; however, each randomized group had only 15 participants and was underpowered to detect changes between groups. Participants in the PAE and TURP groups also had significantly different peak urinary flow rate and bladder contractility scores at baseline. Similarly, the RCT by Insausti et al[16] did not have the required sample size to achieve 80% of power to show noninferiority.

The noninferiority RCT by Abt et al[14] published only interim 12-week results (from a planned 2-year follow-up). The long-term results of this RCT are still pending; however, the authors specified in their protocol that the primary outcome of interest was the change in IPSS at 12 weeks.

The comparative observational studies also had risk-of-bias concerns. There were selective reporting and confounding concerns in the study by Russo et al[17] comparing PAE with OSP. In the Ray et al study, the authors also noted difficulties in recruiting people who had undergone TURP (206 participants in the PAE group and 79 in the TURP group at baseline). The response rate for patient-reported outcomes in Ray et al[15] was also higher for the PAE group (74%) than the TURP group (48%), although a comparison with one hospital site with a high response rate (95%) did not substantially change the findings.

International Prostate Symptom Score

PROSTATIC ARTERY EMBOLIZATION VERSUS TRANSURETHRAL RESECTION OF THE PROSTATE

Five studies evaluated IPSS for PAE compared with TURP and found reductions in IPSS for both PAE and TURP (Table 2).[13-16,39] In general, there was no difference in the mean IPSS results between PAE and TURP at different time points. One study found that mean IPSS results were significantly lower in the TURP group than the PAE group at 3 months; however, the difference was not seen at other later time points (6 months and 1 and 2 years).[13] In contrast, at 1 year, Carnevale et al[39] found that mean IPSS was significantly lower among the TURP and PErFecTED PAE groups compared with the original PAE group (P = .01 and < .001, respectively), but there was no significant difference between the TURP and PErFecTED PAE group (P > .20).

We rated the quality of the evidence for IPSS at 3, 6, and 12 months as very low, downgrading for risk of bias, inconsistency, and imprecision; and low at 24 months, downgrading for risk of bias and imprecision (see Appendix 4, Table A5).

Table 2: International Prostate Symptom Score for Prostatic Artery Embolization Versus Transurethral Resection of the Prostate

		Mean IPSS (95% CI)			Mean IPSS Change From Baseline (95% CI)		
Study	**N**	**PAE**	**TURP**	***P* Value**	**PAE**	**TURP**	***P* Value**
Baseline							
Abt et al, 2018[14]	PAE: 48 TURP: 51	19.4 (17.6–21.2)[a]	17.6 (15.9–19.3)[a]	NR	NA	NA	NA
Carnevale et al, 2016[39]	Original PAE: 15 PErFecTED PAE: 15 TURP: 15	Original: 25.3 (23.5–27.1) PErFecTED: 24.6 (22.8–26.4)	27.6 (26.0–29.2)	.08	NA	NA	NA
Gao et al, 2014[13]	PAE: 54 TURP: 53	24.3 (17.9–30.7)[a]	24.7 (18.5–30.9)[a]	NR	NA	NA	NA
Insausti et al, 2020[16]	PAE: 23 TURP: 22	26.6 (24.1–28.9)[a]	26.9 (23.8–29.9)[a]	NR	NA	NA	NA
Ray et al, 2018[15]	PAE: 216 TURP: 89	21.3 (Median 22.0)	21.6 (Median 22.0)	.926	NA	NA	NA
3 Months							
Abt et al, 2018[14]	PAE: 48 TURP: 51	10.2 (8.2–12.0)[a]	6.8 (5.4–8.3)[a]	.31	−9.2 (−10.8 to −7.7)[b]	−10.8 (−12.3 to −9.2)[b]	.17
Gao et al, 2014[13]	PAE: 54 TURP: 53	15.6 (8.1–23.1)[a]	11.0[a] (6.5–15.6)[a]	< .001	−8.7 (−18.5 to 1.1)[b]	−13.7 (−21.4 to −6.0)[b]	NR
Insausti et al, 2020[16]	PAE: 23 TURP: 22	5.0 (1.7–6.5)[a]	12.6 (8.4–15.7)[a]	NR	−21.6 (−25.0 to −18.2)[b]	−14.3 (−19.1 to −9.5)[b]	NR
Ray et al, 2018[15]	PAE: 159 TURP: 45	9.6 (Median 8.5)	9.8 (Median 5.0)	NR	−11.7 (NR)	−11.8 (NR)	NR
6 Months							
Gao et al, 2014[13]	PAE: 54 TURP: 53	12.8 (7.0–18.7)[a]	11.3 (6.4–16.3)[a]	NS	−11.5 (−20.2 to −2.8)[b]	−13.4 (−21.3 to −5.5)[b]	NR
Insausti et al, 2020[16]	PAE: 23 TURP: 22	4.1 (1.6–5.0)[a]	10.2 (5.7–13.5)[a]	NR	−22.5 (−25.5 to −19.5)[b]	−16.7 (−21.6 to −11.8)[b]	NR
Ray et al, 2018[15]	PAE: 133 TURP: 31	10.1 (Median 9.0)	8.0 (Median 4.0)	NR	−11.2 (NR)	−13.6 (NR)	NR

Study	N	Mean IPSS (95% CI)			Mean IPSS Change From Baseline (95% CI)		
		PAE	TURP	*P* Value	PAE	TURP	*P* Value
12 Months							
Carnevale et al, 2016[39]	Original PAE: 15 PErFecTED PAE: 15 TURP: 15	Original: 12.8 (8.8–16.8) PErFecTED: 3.6 (2.1–5.1)	6.1 (1.7–10.5)	Original PAE vs. TURP: .012 Original PAE vs. PErFecTED: < .001 PErFecTED vs. TURP: > .20	Original: −12.5 (−16.9 to −8.1)[b] PErFecTED: −21.0 (−23.3 to −18.7)[b]	−21.5 (−26.1 to −16.9)[b]	NR, but significant for all groups
Gao et al, 2014[13]	PAE: 54 TURP: 53	10.9[a] (6.8–15.0)	10.2[a] (5.9–14.5)	NS	−13.4 (−21.0 to −5.8)[b]	−14.5 (−22.1 to −6.9)[b]	NR
Insausti et al, 2020[16]	PAE: 23 TURP: 22	5.6[a] (2.4–7.1)	8.8[a] (5.2–10.9)	NR	−21.0 (−23.7 to 18.3)	−18.2 (−21.2 to −15.1)	.08
Ray et al, 2018[15]	PAE: 132 TURP: 29	10.0 (Median 9.0)	7.2 (Median 5.0)	NR	−10.9 (Median −10.0) N = 117 *P* < .001	−15.2 (Median −15.0) N = 21 *P* < .001	> .05[c]
24 Months							
Gao et al, 2014[13]	PAE: 47 TURP: 48	8.7[a] (4.6–12.8)	8.4[a] (4.2–12.6)	NS	−15.6 (−23.6 to −7.6)[b]	−16.3 (−24.1 to −8.5)[b]	NR

Abbreviations: CI, confidence interval; IPSS, International Prostate Symptom Score; NA, not applicable; NR, not reported; NS, not significant; PAE, prostatic artery embolization; PErFecTED, proximal embolization first then embolize distal method of PAE; TURP, transurethral resection of the prostate.
[a]Estimated 95% confidence intervals were extracted from graphs using WebPlotDigitizer.[34]
[b]Change from baseline was calculated and the corresponding standard deviation was imputed.
[c]Non-inferiority testing was done for IPSS changes of 2.0, 3.0, and 4.0 and all *P* values were > .05, thereby rejecting the null hypothesis and showing no evidence that PAE is non-inferior to TURP.

PROSTATIC ARTERY EMBOLIZATION VERSUS OPEN SIMPLE PROSTATECTOMY

Open simple prostatectomy led to significantly lower mean IPSS results at both 6 months and 1 year compared with PAE (Table 3).[17] When adjusted for preoperative and perioperative variables, Russo et al[17] found that PAE was associated with a 2.67-fold increase in 1-year persistent symptoms (IPSS ≥ 8).

We rated the quality of the evidence for IPSS at 6 and 12 months as very low, downgrading for risk of bias and imprecision (see Appendix 4, Table A5).

Table 3: International Prostate Symptom Score for Prostatic Artery Embolization Versus Open Simple Prostatectomy

		Mean IPSS (95% CI)			Mean IPSS Change from Baseline (95% CI)		
Study	**N**	**PAE**	**OSP**	***P* Value**	**PAE**	**OSP**	***P* Value**
Baseline							
Russo et al, 2015[17]	PAE: 80 OSP: 80	24.0 (22.7–25.3)	23.4 (22.3–24.4)	.53	NA	NA	NA
6 Months							
Russo et al, 2015[17]	PAE: 80 OSP: 80	11.4 (10.7–12.0)	4.9 (4.2–5.7)	< .01	−12.6 (−14.1 to −11.2)[a]	−18.4 (−19.7 to −17.2)[a]	NR
12 Months							
Russo et al, 2015[17]	PAE: 80 OSP: 80	10.4 (9.4–11.4)	4.3 (3.6–5.0)	< .01	−13.6 (−15.2 to −11.9)[a]	−19.0 (−20.3 to −17.8)[a]	< .05

Abbreviations: CI, confidence interval; IPSS, International Prostate Symptom Score; NA, not applicable; NR, not reported; OSP, open simple prostatectomy; PAE, prostatic artery embolization.
[a]Change from baseline was calculated and the corresponding standard deviation was imputed.

Health-Related Quality of Life

PROSTATIC ARTERY EMBOLIZATION VERSUS TRANSURETHRAL RESECTION OF THE PROSTATE

All five studies that evaluated health-related quality of life used the IPSS–Quality of Life scale (Table 4).[13-16,39] A decrease in IPSS–Quality of Life scores indicate improved quality of life. In general, quality of life improved for both PAE and TURP groups, and results were similar between groups.

We rated the quality of the evidence for health-related quality of life at 3 and 12 months as very low, downgrading for risk of bias, inconsistency, and imprecision; and low at 6 and 24 months, downgrading for risk of bias and imprecision (see Appendix 4, Table A5).

Table 4: Health-Related Quality of Life for Prostatic Artery Embolization Versus Transurethral Resection of the Prostate

		Mean IPSS–QoL (95% CI)			Mean IPSS–QoL Change from Baseline (95% CI)		
Study	**N**	**PAE**	**TURP**	***P* Value**	**PAE**	**TURP**	***P* Value**
Baseline							
Abt et al, 2018[14]	PAE: 48 TURP: 51	4.0 (3.7–4.3)[a]	4.2 (3.9–4.6)[a]	NR	NA	NA	NA
Carnevale et al, 2016[39]	Original PAE: 15 PErFecTED PAE: 15 TURP: 15	Original: 4.7 (4.4–5.0) PErFecTED: 4.7 (4.4–5.0)	4.6 (4.2–5.0)	> .2	NA	NA	NA
Gao et al, 2014[13]	PAE: 54 TURP: 53	4.8 (4.0–5.6)[a]	4.6 (3.9–5.3)[a]	NS	NA	NA	NA
Insausti et al, 2020[16]	PAE: 23 TURP: 22	4.5 (4.1–4.9)[a]	4.7 (4.3–5.2)[a]	NR	NA	NA	NA
Ray et al, 2018[15]	PAE: 189 TURP: 48	4.6 (Median 5.0)	4.9 (Median 5.0)	.076	NA	NA	NA
3 Months							
Abt et al, 2018[14]	PAE: 48 TURP: 51	1.7 (1.2–2.1)[a]	1.6 (1.1–2.0)[a]	.2	−2.3 (−4.2 to −0.5)	−2.7 (−4.4 to −0.9)	NR
Gao et al, 2014[13]	PAE: 54 TURP: 53	2.9 (1.9–3.9)[a]	2.3 (1.3–3.3)[a]	< .001	−1.9 (−3.2 to −0.6)[b]	−2.3 (−3.5 to −1.1)[b]	NR
Insausti et al, 2020[16]	PAE: 23 TURP: 22	0.9 (0.5–1.3)[a]	2.1 (1.5–2.7)[a]	NR	−3.6 (-4.2 to −3.0)[b]	−2.6 (−3.4 to −1.9)[b]	NR
Ray et al, 2018[15]	PAE: 160 TURP: 46	1.9 (Median 2.0)	1.9 (Median 2.0)	NR	−2.7 (NR)	−3.0 (NR)	NR
6 Months							
Gao et al, 2014[13]	PAE: 54 TURP: 53	2.2 (1.1–3.3)[a]	2.3 (1.4–3.2)[a]	NS	−2.6 (−4.0 to −1.2)[b]	−2.3 (−3.4 to −1.2)[b]	NR
Insausti et al, 2020[16]	PAE: 23 TURP: 22	0.7 (0.3–1.0)[a]	1.7 (1.0–2.3)[a]	NR	−3.8 (-4.4 to −3.3)[b]	−3.1 (−3.8 to −2.3)[b]	NR
Ray et al, 2018[15]	PAE: 135 TURP: 35	2.1 (Median 2.0)	1.9 (Median 1.0)	NR	−2.5 (NR)	−3.0 (NR)	NR
12 Months							
Carnevale et al, 2016[39]	Original PAE: 15 PErFecTED PAE: 15 TURP: 15	Original: 2.2 (1.6–2.8) PErFecTED: 1.6 (1.2–2.0)	0.9 (0.2–1.6)	NR	Original: −2.5 (−3.2 to −1.8)[b] PErFecTED: −3.1 (−3.6 to −2.6)[b]	−3.7 (−4.5 to −2.9)[b]	NR
Gao et al, 2014[13]	PAE: 54 TURP: 53	1.9 (1.0–2.8)[a]	1.8 (0.9–2.7)[a]	NS	−2.9 (−4.1 to −1.7)[b]	−2.8 (−3.9 to −1.7)[b]	NR

Study	N	Mean IPSS–QoL (95% CI)			Mean IPSS–QoL Change from Baseline (95% CI)		
		PAE	TURP	*P* Value	PAE	TURP	*P* Value
Insausti et al, 2020[16]	PAE: 23 TURP: 22	0.7 (0.4–1.0)[a]	1.6 (1.2–2.1)[a]	NR	−3.8 (−4.3 to −3.2)	−3.1 (−3.7 to −2.5)	.002
Ray et al, 2018[15]	PAE: 133 TURP: 31	2.0 (Median 2.0)	1.5 (Median 1.0)	NR	−2.6 (Median −3.0) N = 126 *P* < .001	−3.4 (Median 4.0) N = 26 *P* < .001	> .05[c]
24 Months							
Gao et al, 2014[13]	PAE: 47 TURP: 48	1.6 (0.7–2.5)[a]	1.4 (0.6–2.2)[a]	NS	−3.2 (−4.4 to −2.0)[b]	−3.2 (−4.3 to −2.1)[b]	NR

Abbreviations: CI, confidence interval; IPSS, International Prostate Symptom Score–Quality of Life; NA, not applicable; NR, not reported; NS, not significant; PAE, prostatic artery embolization; PErFecTED, proximal embolization first then embolize distal method of PAE; TURP, transurethral resection of the prostate.
[a]Estimated 95% confidence intervals were extracted from graphs using WebPlotDigitizer.[34]
[b]Change from baseline was calculated and the corresponding standard deviation was imputed.
[c]Noninferiority testing was done for IPSS–QOL changes of 0.75, 1.0, and 1.25 between PAE and TURP. *P* values for changes of 0.75 or 1.0 were > .05, thereby rejecting the null hypothesis and showing no evidence that PAE is noninferior to TURP. An IPSS–QOL change of 1.25 had a *P* value of .015, thereby accepting the null hypothesis and showing that PAE is noninferior to TURP; however, the authors deemed this noninferiority margin too large for the narrow six-point IPSS–QOL scale.

PROSTATIC ARTERY EMBOLIZATION VERSUS OPEN SIMPLE PROSTATECTOMY

Open simple prostatectomy led to significantly improved mean IPSS–Quality of Life scores at 1 year compared with PAE (Table 5).[17]

We rated the quality of the evidence for health-related quality of life at 12 months as very low, downgrading for risk of bias and imprecision (see Appendix 4, Table A5).

Table 5: Health-Related Quality of Life for Prostatic Artery Embolization Versus Open Simple Prostatectomy

Study	N	Mean IPSS–QoL (95% CI)			Mean IPSS–QoL Change from Baseline (95% CI)		
		PAE	OSP	*P* Value	PAE	OSP	*P* Value
Baseline							
Russo et al, 2015[17]	PAE: 80 OSP: 80	4.4 (4.2–4.6)	4.1 (3.9–4.3)	.1	NA	NA	NA
12 Months							
Russo et al, 2015[17]	PAE: 80 OSP: 80	2.8 (2.6–3.0)	0.7 (0.6–0.9)	< .01	−1.6 (−1.9 to −1.3)[a]	−3.4 (−3.6 to −3.1)[a]	< .05

Abbreviations: CI, confidence interval; IPSS, International Prostate Symptom Score; NA, not applicable; OSP, open simple prostatectomy; PAE, prostatic artery embolization; QOL, quality of life.
[a]Change from baseline was calculated and the corresponding standard deviation was imputed.

Erectile Function

PROSTATIC ARTERY EMBOLIZATION VERSUS TRANSURETHRAL RESECTION OF THE PROSTATE

All but one study used a shortened five-question version of the International Index of Erectile Function (known as the IIEF-5).[14,15,39] Possible scores for the IIEF-5 range from 5 to 25, and erectile dysfunction is

classified into five categories based on score: severe (5–7), moderate (8–11), mild to moderate (12–16), mild (17–21), and no erectile dysfunction (22–25). Insausti et al[16] used IIEF-6 (a six-question version of the IIEF); however, according to the study authors, erectile function could not be assessed because too few participants had actively sexual relationships due to participants' higher mean age.[16]

The results for erectile function for PAE compared with TURP are presented in Table 6. Carnevale et al[39] found a significant increase in erectile dysfunction in the TURP group at 12 months, but not in the two PAE groups (original or PErFecTED). However, these results are likely affected by baseline differences in IIEF as participants in the PErFecTED group had significantly higher IIEF scores than those in the TURP group (P = .015). In contrast, the other two studies found no difference in erectile function between PAE and TURP at various time points.[14,15]

We rated the quality of the evidence for erectile function at 3 and 12 months as very low, downgrading for risk of bias, inconsistency, and imprecision; and at 6 months as very low, based on one nonrandomized study, downgrading for risk of bias and imprecision (see Appendix 4, Table A5).

Table 6: Erectile Function for Prostatic Artery Embolization Versus Transurethral Resection of the Prostate

Study	N	Mean IIEF-5 (95% CI)			Mean IIEF-5 Change From Baseline (95% CI)		
		PAE	TURP	*P* Value	PAE	TURP	*P* Value
Baseline							
Abt et al, 2018[14]	PAE: 48 TURP: 51	15.2 (12.9–17.4)	13.1 (10.9–15.4)	NR	NA	NA	NA
Carnevale et al, 2016[39]	Original PAE: 15 PErFecTED PAE: 15 TURP: 15	Original: 14.3 (10.9–17.7) PErFecTED: 17.3 (14.6–20.0)	12.5 (9.2–15.8)	.05	NA	NA	NA
Ray et al, 2018[15]	PAE: 164 TURP: 36	14.4 (Median 15.0)	14.4 (Median 15.0)	.906	NA	NA	NA
3 Months							
Abt et al, 2018[14]	PAE: 48 TURP: 51	14.6 (12.1–17.2)[a]	11.7 (9.1–14.2)[a]	.5	−0.5 (−3.7 to 2.6)[b]	−1.4 (−4.5 to 1.7)[b]	NR
Ray et al, 2018[15]	PAE: 126 TURP: 28	16.2 (Median 18.0)	15.6 (Median 16.0)	NR	1.8 (NR)	1.2 (NR)	NR
6 Months							
Ray et al, 2018[15]	PAE: 100 TURP: 20	17.0 (Median 19.0)	19.2 (Median 20.0)	NR	2.6 (NR)	4.8 (NR)	NR
12 Months							
Carnevale et al, 2016[39]	Original PAE: 15 PErFecTED PAE: 15 TURP: 15	Original: 12.6 (9.7–15.5) PErFecTED: 18.7 (17.1–20.3)	16.1 (13.2–19.0)	NR	Original: −1.7 (−6.2 to 2.8)[b] PErFecTED: 1.4 (−1.7 to 4.5)[b]	3.6 (−0.8 to 8.0)[b]	NR
Ray et al, 2018[15]	PAE: 102 TURP: 20	16.3 (Median 19.0)	14.8 (Median 13.5)	NR	1.0 (Median 0) N = 94 *P* = .19	−0.2 (Median 0) N = 15 *P* = .90	NR

Abbreviations: CI, confidence interval; IIEF, International Index of Erectile Function; NA, not applicable; NR, not reported; PAE, prostatic artery embolization; PErFecTED, proximal embolization first then embolize distal method of PAE; TURP, transurethral resection of the prostate.
[a]Estimated 95% confidence intervals were extracted from graphs using WebPlotDigitizer.[34]
[b]Change from baseline was calculated and the corresponding standard deviation was imputed.

PROSTATIC ARTERY EMBOLIZATION VERSUS OPEN SIMPLE PROSTATECTOMY

Prostatic artery embolization was found to result in better erectile function using IIEF-5, at both 6 months and 1 year compared with OSP (Table 7).[17]

We rated the quality of the evidence for erectile function at 6 and 12 months as very low, downgrading for risk of bias and imprecision (see Appendix 4, Table A5).

Table 7: Erectile Function for Prostatic Artery Embolization Versus Open Simple Prostatectomy

Study	N	Mean IIEF-5 (95% CI)			Mean IIEF-5 From Baseline (95% CI)		
		PAE	OSP	*P* Value	PAE	OSP	*P* Value
Baseline							
Russo et al, 2015[17]	PAE: 80 OSP: 80	14.5 (13.4–15.5)	15.1 (13.8–16.4)	.56	NA	NA	NA
6 Months							
Russo et al, 2015[17]	PAE: 80 OSP: 80	15.5 (14.4–16.7)	10.7 (9.0–12.4)	< .01	1.1 (−0.5 to 2.6)[a]	−4.4 (−6.6 to −2.2)[a]	NR
12 Months							
Russo et al, 2015[17]	PAE: 80 OSP: 80	15.1 (14.0–16.2)	10.9 (9.2–12.6)	< .01	0.7 (−0.9 to 2.2)[a]	−4.2 (−6.4 to −2.1)[a]	NR

Abbreviations: CI, confidence interval; IIEF, International Index of Erectile Function; NA, not applicable; NR, not reported; OSP, open simple prostatectomy; PAE, prostatic artery embolization.
[a]Change from baseline was calculated and the corresponding standard deviation was imputed.

Peak (Maximum) Urinary Flow

PROSTATIC ARTERY EMBOLIZATION VERSUS TRANSURETHRAL RESECTION OF THE PROSTATE

All studies found an increase in mean peak urinary flow rate from baseline for TURP compared with PAE (Table 8).[13,14,16,39] The was a significant improvement in mean peak urinary flow rate in the short-term (at 3 months) for TURP compared with PAE in two studies[13,14]. At one year or later, mean peak urinary flow rate was generally similar between PAE and TURP.

We rated the quality of the evidence for peak urinary flow rate at 3, 6, 12, and 24 months as low, downgrading for risk of bias and imprecision (see Appendix 4, Table A5).

Table 8: Peak Urinary Flow for Prostatic Artery Embolization Versus Transurethral Resection of the Prostate

Study	N	Mean Q_{max}, mL/s (95% CI)			Mean Q_{max} Change From Baseline, mL/S (95% CI)		
		PAE	TURP	*P* Value	PAE	TURP	*P* Value
Baseline							
Abt et al, 2018[14]	PAE: 48 TURP: 51	7.5 (6.2–8.6)[a]	7.3 (5.9–8.5)[a]	NR	NA	NA	NA
Carnevale et al, 2016[39]	Original PAE: 15 PErFecTED PAE: 15 TURP: 15	Original: 7.0 (5.2–8.8) PErFecTED: 5.1 (3.6–6.6)	9.7 (7.8–11.6)	.004	NA	NA	NA
Gao et al, 2014[13]	PAE: 54 TURP: 53	7.8 (5.3–10.3)[a]	7.3 (5.0–9.6)[a]	NS	NA	NA	NA
Insausti et	PAE: 23	7.7	7.0	NR	NA	NA	NA

Study	N	Mean Q_{max}, mL/s (95% CI)			Mean Q_{max} Change From Baseline, mL/S (95% CI)		
		PAE	TURP	*P* Value	PAE	TURP	*P* Value
al, 2020[16]	TURP: 22	(6.6–8.8)[a]	(5.9–8.2)[a]				
Ray et al, 2018[15]	PAE: 132 TURP: 39	8.8 (Median 8.0)	10.4 (Median 10.0)	.095	NA	NA	NA
3 Months							
Abt et al, 2018[14]	PAE: 48 TURP: 51	13.0 (11.3–14.7)[a]	22.5 (18.5–26.4)[a]	< .001	5.5 (3.1–8.0)[b]	15.3 (11.0–19.6)[b]	NR
Gao et al, 2014[13]	PAE: 54 TURP: 53	17.3 (13.6–21.4)[a]	21.4 (16.6–26.2)[a]	< .001	9.5 (4.9–14.1)[b]	14.1 (8.8–19.4)[b]	NR
Insausti et al, 2020[16]	PAE: 23 TURP: 22	12.3 (10.6–14.5)[a]	14.0 (10.9–18.4)[a]	NR	4.6 (2.4–6.8)[b]	7.0 (3.0–10.9)[b]	NR
Ray et al, 2018[15]	PAE: 115 TURP: 21	13.6 (Median 12.0)	20.8 (Median 19.0)	NR	4.8 (NR)	10.4 (NR)	NR
6 Months							
Gao et al, 2014[13]	PAE: 54 TURP: 53	21.5 (17.3–25.7)[a]	23.7 (20.4–27.0)[a]	NS	13.7 (8.8–18.6)[b]	16.4 (12.4–20.4)[b]	NR
Insausti et al, 2020[16]	PAE: 23 TURP: 22	13.5 (11.9–15.3)[a]	13.3 (9.6–16.2)[a]	NR	5.8 (3.8–7.9)[b]	6.3 (2.8–9.8)[b]	NR
12 Months							
Carnevale et al, 2016[39]	Original PAE: 15 PErFecTED PAE: 15 TURP: 15	Original: 10.1 (6.8–13.4) PErFecTED: 8.4 (12.4–21.0)	27.1 (22.7–31.5)	NR	Original: 3.1 (−0.7 to 6.9)[b] PErFecTED: 11.6 (7.1–16.1)[b]	17.4 (12.6–22.2)[b]	NR
Gao et al, 2014[13]	PAE: 54 TURP: 53	22.1 (18.6–25.6)[a]	23.1 (19.9–26.4)[a]	NS	14.3 (10.0–18.6)[b]	15.8 (11.8–19.8)[b]	NR
Insausti et al, 2020[16]	PAE: 23 TURP: 22	13.8 (11.9–14.5)[a]	16.7 (12.2–19.2)[a]	NR	6.1 (4.0–8.3	9.7 (5.4–13.9)	.862
Ray et al, 2018[15]	PAE: 106 TURP: 13	14.1 (Median 13.5)	22.3 (Median 20.0)	NR	4.4 (Median 3.0) N = 78 *P* < .001	8.6 (Median 7.5) N = 10 *P* = .022	NR
24 Months							
Gao et al, 2014[13]	PAE: 47 TURP: 48	21.5 (17.9–25.1)[a]	22.1 (18.6–25.6)[a]	NS	13.7 (9.2–18.2)[b]	14.8 (10.5–19.1)[b]	NR

Abbreviations: CI, confidence interval; NA, not applicable; NR, not reported; NS, not significant; PAE, prostatic artery embolization; PErFecTED, proximal embolization first then embolize distal method of PAE; Q_{max}, peak (maximum) urinary flow rate; TURP, transurethral resection of the prostate.
[a]Estimated 95% confidence intervals were extracted from graphs using WebPlotDigitizer.[34]
[b]Change from baseline was calculated and the corresponding standard deviation was imputed.

PROSTATIC ARTERY EMBOLIZATION VERSUS OPEN SIMPLE PROSTATECTOMY

Russo et al[17] found that OSP led to significantly lower mean peak urinary flow rates at both 6 months and 1 year compared with PAE (Table 9). When adjusted for preoperative and perioperative variables, the authors found that PAE was associated with a five-fold increase for persistent peak urinary flow rates equal to or less than 15 mL/s at 1 year.

We rated the quality of the evidence for peak urinary flow rate at 6 and 12 months as very low, downgrading for risk of bias and imprecision (see Appendix 4, Table A5).

Table 9: Peak Urinary Flow for Prostatic Artery Embolization Versus Open Simple Prostatectomy

		Mean Q_{max}, mL/s (95% CI)			Mean Q_{max} From Baseline, mL/s (95% CI)		
Study	**N**	**PAE**	**OSP**	***P* Value**	**PAE**	**OSP**	***P* Value**
Baseline							
Russo et al, 2015[17]	PAE: 80 OSP: 80	7.3 (6.5–8.0)	7.9 (7.5–8.2)	.21	NA	NA	NA
6 Months							
Russo et al, 2015[17]	PAE: 80 OSP: 80	16.2 (15.2–17.2)	24.5 (23.3–25.7)	< .01	9.0 (7.8–10.2)[a]	16.7 (15.4–17.9)[a]	NR
12 Months							
Russo et al, 2015[17]	PAE: 80 OSP: 80	16.9 (15.8–18.0)	23.8 (22.5–25.1)	< .01	9.6 (8.3–10.9)[a]	16.0 (14.6–17.3)[a]	NR

Abbreviations: CI, confidence interval; NA, not applicable; NR, not reported; OSP, open simple prostatectomy; PAE, prostatic artery embolization; Q_{max}, peak (maximum) urinary flow rate.
[a]Change from baseline was calculated and the corresponding standard deviation was imputed.

Post-Void Residual Volume

PROSTATIC ARTERY EMBOLIZATION VERSUS TRANSURETHRAL RESECTION OF THE PROSTATE
Five studies evaluated post-void residual volume for PAE compared with TURP (Table 10).[13-16,39] Reductions in post-void residual volume was generally higher for TURP than PAE, although the significance of these differences was not consistently reported. Two studies found a significant reduction in mean post-void residual volume for TURP compared with PAE at 3 months.[13,14] At 1 year, post-void residual volume reduced by about 16–100 mL in the PAE group and about 78–120 mL in the TURP group. Gao et al[13] found no difference in post-void residual volumes for PAE and TURP at 2 years.

We rated the quality of the evidence for post-void residual volume at 3 and 12 months as very low, downgrading for risk of bias, inconsistency, and imprecision, and as low at 6 and 24 months, downgrading for risk of bias and imprecision (see Appendix 4, Table A5).

Table 10: Post-Void Residual Volume for Prostatic Artery Embolization Versus Transurethral Resection of the Prostate

		Mean PVR, mL (95% CI)			Mean PVR Change from Baseline, mL (95% CI)		
Study	**N**	**PAE**	**TURP**	***P* Value**	**PAE**	**TURP**	***P* Value**
Baseline							
Abt et al, 2018[14]	PAE: 48 TURP: 51	168.5 (116.2–220.0)	230.7 (172.2–289.7)	NR	NA	NA	NA
Carnevale et al, 2016[39]	Original PAE: 15 PErFecTED	Original: 78.3 (41.2–115.4) PErFecTED:	127.0 (76.4–177.6)	> .2	NA	NA	NA

Study	N	Mean PVR, mL (95% CI)			Mean PVR Change from Baseline, mL (95% CI)		
		PAE	TURP	*P* Value	PAE	TURP	*P* Value
	PAE: 15 TURP: 15	74.2 (49.3–99.1)					
Gao et al, 2014[13]	PAE: 54 TURP: 53	126.9 (57.9–195.7)[a]	115.4 (46.3–184.4)[a]	NS	NA	NA	NA
Insausti et al, 2020[16]	PAE: 23 TURP: 22	82.3 (0.5–164.8)[a]	124.4 (55.0–194.6)[a]	NS	NA	NA	NA
Ray et al, 2018[15]	PAE: 125 TURP: 46	161.6 (Median 130.0)	263.6 (Median 204.0)	.004	NA	NA	NA
3 Months							
Abt et al, 2018[14]	PAE: 48 TURP: 51	70.3 (43.7–97.7)[a]	33.7 (21.2–45.8)[a]	.003	−98.2 (−125.3 to −71.1)[b]	−197.0 (−209.4 to −184.6)[b]	NR
Gao et al, 2014[13]	PAE: 54 TURP: 53	56.8 (17.4–95.8)[a]	33.2 (6.5–56.8)[a]	.012	−70.1 (−149.4 to 9.2)[b]	−82.2 (−155.7 to −8.7)[b]	NR
Insausti et al, 2020[16]	PAE: 23 TURP: 22	21.1 (10.2–33.0)[a]	22.6 (14.7–31.2)[a]	NR	−61.2 (−144.1 to 21.7)[b]	−101.8 (−172.1 to −31.5)[b]	NR
Ray et al, 2018[15]	PAE: 110 TURP: 20	126.2 (Median 97.0)	88.8 (Median 56.5)	NR	−35.4 (NR)	−174.8 (NR)	NR
6 Months							
Gao et al, 2014[13]	PAE: 54 TURP: 53	39.2 (9.0–69.1)[a]	30.9 (5.4–56.1)[a]	NS	−87.7 (−162.9 to −12.5)[b]	−84.5 (−158.1 to −10.9)[b]	NR
Insausti et al, 2020[16]	PAE: 23 TURP: 22	15.1 (7.8–23.4)[a]	18.9 (8.0–30.8)[a]	NR	−67.2 (−149.7 to 15.3)[b]	−105.5 (−176.2 to −34.8)[b]	NR
12 Months							
Carnevale et al, 2016[39]	Original PAE: 15 PErFecTED PAE: 15 TURP: 15	Original: 62.3 (26.4–98.2) PErFecTED: 48.6 (15.4–81.8)	8.3 (2.3–14.3)	NR	Original: −16.0 (−67.6 to 35.6)[b] PErFecTED: −25.6 (−67.2 to 16.0)[b]	−118.7 (−169.6 to −67.8)[b]	NR
Gao et al, 2014[13]	PAE: 54 TURP: 53	27.3 (3.3–51.0)[a]	22.3 (4.7–39.8)[a]	NS	−99.6 (−172.5 to −26.7)[b]	−93.1 (−164.4 to −21.8)[b]	NR
Insausti et al, 2020[16]	PAE: 23 TURP: 22	13.1 (4.9–22.3)[a]	15.0 (10.2–20.9)[a]	NR	−69.2 (−151.8 to 13.4)	−109.4 (−179.4 to −39.4)	.67
Ray et al, 2018[15]	PAE: 101 TURP: 13	129.6 (Median 120.0)	80.6 (Median 48.0)	NR	−40.4 (Median −15.0) N = 70 *P* = .071	−78.1 (Median −48.5) N = 12 *P* = .059	NR
24 Months							
Gao et al, 2014[13]	PAE: 47 TURP: 48	19.4 (4.0–34.4)[a]	15.2 (2.2–27.8)[a]	NS	−107.5 (−182.9 to −32.1)[b]	−100.2 (−173.9 to −26.5)[b]	NR

Abbreviations: CI, confidence interval; NA, not applicable; NR, not reported; NS, not significant; PAE, prostatic artery embolization; PErFecTED, proximal embolization first then embolize distal method of PAE; PVR, post-void residual volume; TURP, transurethral resection of the prostate.
[a]Estimated 95% confidence intervals were extracted from graphs using WebPlotDigitizer.[34]
[b]Change from baseline was calculated and the corresponding standard deviation was imputed.

PROSTATIC ARTERY EMBOLIZATION VERSUS OPEN SIMPLE PROSTATECTOMY

Open simple prostatectomy was found to result in significantly lower post-void residual volume at both 6 months and 1 year compared with PAE (Table 11).[17] We rated the quality of the evidence for post-void residual volume at 6 and 12 months as very low, downgrading for risk of bias and imprecision (see Appendix 4, Table A5).

Table 11: Post-Void Residual Volume for Prostatic Artery Embolization Versus Open Simple Prostatectomy

		Mean PVR, mL (95% CI)			Mean PVR From Baseline, mL (95% CI)		
Study	**N**	**PAE**	**OSP**	**P-Value**	**PAE**	**OSP**	**P-Value**
Baseline							
Russo et al, 2015[17]	PAE: 80 OSP: 80	64.3 (57.0–71.5)	65.0 (51.0–78.9)	.95	NA	NA	NA
6 Months							
Russo et al, 2015[17]	PAE: 80 OSP: 80	19.2 (17.0–21.4)	4.3 (3.4–5.2)	< .01	−45.0 (−52.6 to −37.4)[a]	−60.6 (−74.6 to −46.7)[a]	NR
12 Months							
Russo et al, 2015[17]	PAE: 80 OSP: 80	18.4 (16.3–20.5)	6.2 (5.2–7.1)	< .01	−45.9 (−53.4 to −38.3)[a]	−58.8 (−72.7 to −44.9)[a]	NR

Abbreviations: CI, confidence interval; NA, not applicable; NR, not reported; OSP, open simple prostatectomy; PAE, prostatic artery embolization; PVR, post-residual volume.

[a]Change from baseline was calculated and the corresponding standard deviation was imputed.

Prostate Volume

PROSTATIC ARTERY EMBOLIZATION VERSUS TRANSURETHRAL RESECTION OF THE PROSTATE

Five studies evaluated the changes in prostate volume between PAE and TURP (Table 12).[13-16,39] All studies found lower prostate volumes for TURP compared with PAE, although the significance of the difference between the two groups was not reported in the studies for all time points. In one study, there were baseline differences in prostate volume, with participants in the PAE group having significantly larger prostate volumes initially than the TURP group.[15]

At 1 year, the mean reduction in prostate volume was about 6 mL to 30 mL for PAE and about 30 mL to 45 mL for TURP. Gao et al[13] noted significantly reduced prostate volumes favouring TURP at 2 years (30 mL for PAE vs. 37 mL for TURP).

We rated the quality of the evidence for prostate volume at 3, 6, 12, and 24 months as low, downgrading for risk of bias and imprecision (see Appendix 4, Table A5).

Table 12: Prostate Volume for Prostatic Artery Embolization Versus Transurethral Resection of the Prostate

		Mean PV, mL (95% CI)			Mean PV Change From Baseline, mL (95% CI)		
Study	**N**	**PAE**	**TURP**	***P* Value**	**PAE**	**TURP**	***P* Value**
Baseline							
Abt et al, 2018[14]	PAE: 48 TURP: 51	52.8 (43.8–61.9)[a]	56.5 (48.0–65.0)[a]	NR	NA	NA	NA
Carnevale et al, 2016[39]	Original PAE: 15 PErFecTED PAE: 15 TURP: 15	Original: 56.6 (45.7–67.5) PErFecTED: 66.2 (59.8–72.6)	63.0 (54.0–72.0)	> .2	NA	NA	NA
Gao et al, 2014[13]	PAE: 54 TURP: 53	64.7 (44.8–84.2)[a]	63.5 (44.8–81.9)[a]	NS	NA	NA	NA
Insausti et al, 2020[16]	PAE: 23 TURP: 22	60.0 (51.3–68.7)[a]	62.9 (52.9–72.8)[a]	NR	NA	NA	NA
Ray et al, 2018[15]	PAE: 209 TURP: 28	101.2 (Median 89.0)	65.6 (Median 58.5)	< .01	NA	NA	NA
3 Months							
Abt et al, 2018[14]	PAE: 48 TURP: 51	40.7 (33.9–47.6)[a]	27.2 (22.2–31.5)[a]	< .001	−12.2 (−19.2 to −5.1)[b]	−29.3 (−34.3 to −24.4)[b]	NR
Gao et al, 2014[13]	PAE: 54 TURP: 53	43.4 (25.8–60.6)[a]	27.3 (14.5–39.8)[a]	< .001	−21.3 (−47.6 to 5.0)[b]	−36.2 (−58.7 to −13.7)[b]	NR
Insausti et al, 2020[16]	PAE: 23 TURP: 22	40.1 (33.4–47.0)[a]	21.7 (18.5–25.0)[a]	NR	−19.9 (−31.0 to −8.8)[b]	−41.2 (−51.6 to −30.8)[b]	NR
Ray et al, 2018[15]	PAE: 192 TURP: 3	72.1 (Median 60.0)	58.7 (Median 49.0)	NR	−29.1 (NR)	−6.8 (NR)	NR
6 Months							
Gao et al, 2014[13]	PAE: 54 TURP: 53	36.3 (23.1–49.4)[a]	26.8 (15.2–38.2)[a]	< .001	−28.4 (−52.1 to −4.7)[b]	−36.7 (−58.5 to −14.9)[b]	NR
Insausti et al, 2020[16]	PAE: 23 TURP: 22	37.7 (31.3–44.1)[a]	19.9 (16.4–23.7)[a]	NR	−22.3 (−33.1 to −11.5)[b]	−43.0 (−53.6 to −32.4)[b]	NR
12 Months							
Carnevale et al, 2016[39]	Original PAE: 15 PErFecTED PAE: 15 TURP: 15	Original: 50.9 (41.3–60.5) PErFecTED: 50.0 (43.0–57.0)	32.0 (26.2–37.8)	NR	Original: −5.7 (−20.2 to 8.8)[b] PErFecTED: −16.2 (−25.7 to −6.7)[b]	−31.0 (−41.7 to −20.3)[b]	NR
Gao et al, 2014[13]	PAE: 54 TURP: 53	35.6 (22.6–48.4)[a]	26.4 (15.6–36.8)[a]	< .001	−29.1 (−52.6 to −5.6)[b]	−37.1 (−58.4 to −15.8)[b]	NR
Insausti et al, 2020[16]	PAE: 23 TURP: 22	39.5 (31.7–47.4)	18.2 (15.2–21.2)	NR	−20.5 (−32.2 to −8.8)	−44.7 (−55.1 to −34.3)	< .001
Ray et al, 2018[15]	PAE: 166 TURP: 0	72.8 (Median 58.0)	NA	NA	−28.6 (Median −25.0) N = 165 P < .001	NA	NA

Study	N	Mean PV, mL (95% CI)			Mean PV Change From Baseline, mL (95% CI)		
		PAE	TURP	*P* Value	PAE	TURP	*P* Value
24 Months							
Gao et al, 2014[13]	PAE: 47 TURP: 48	34.9 (21.1–48.4)[a]	26.6 (16.1–36.8)[a]	< .001	−29.8 (−54.9 to −4.7)[b]	−36.9 (−59.0 to −14.8)[b]	NR

Abbreviations: CI, confidence interval; NA, not applicable; NR, not reported; NS, not significant; PAE, prostatic artery embolization; PErFecTED, proximal embolization first then embolize distal method of PAE; PV, prostate volume; TURP, transurethral resection of the prostate.
[a]Estimated 95% confidence intervals were extracted from graphs using WebPlotDigitizer.[34]
[b]Change from baseline was calculated and the corresponding standard deviation was imputed.

PROSTATIC ARTERY EMBOLIZATION VERSUS OPEN SIMPLE PROSTATECTOMY

Russo et al[17] did not report on changes in prostate volume between PAE and OSP.

Prostate-Specific Antigen Level

PROSTATIC ARTERY EMBOLIZATION VERSUS TRANSURETHRAL RESECTION OF THE PROSTATE

Four studies evaluated changes in PSA levels between PAE and TURP (Table 13).[13,14,16,39] In general, all studies found a greater reduction in mean PSA levels in the TURP group compared with PAE at different time points, but the difference was not always statistically significant. Two studies[13,16] found significantly greater reductions in PSA levels in the TURP group compared to PSA at 1 year; however, one small-sized study[39] found similar changes between groups. Prostate-specific antigen levels at 2 years was still significantly more reduced in the TURP group compared with PAE, according to one study.[13]

We rated the quality of the evidence for PSA level at 3 months as very low, downgrading for risk of bias, indirectness, inconsistency, and imprecision; and very low at 6, 12, and 24 months, downgrading for risk of bias, indirectness, and imprecision (see Appendix 4, Table A5).

Table 13: Prostate-Specific Antigen Level for Prostatic Artery Embolization Versus Transurethral Resection of the Prostate

Study	N	Mean PSA (95% CI)			Mean PSA Change From Baseline (95% CI)		
		PAE	TURP	*P* Value	PAE	TURP	*P* Value
Baseline							
Abt et al, 2018[14]	PAE: 48 TURP: 51	4.2 (2.6–5.7)	4.5 (3.0–6.0)	.1	NA	NA	NA
Carnevale et al, 2016[39]	Original PAE: 15 PErFecTED PAE: 15 TURP: 15	Original: 3.4 (2.3–4.5) PErFecTED: 3.7 (2.6–4.8)	3.2 (1.9–4.5)	> .2	NA	NA	NA
Gao et al, 2014[13]	PAE: 54 TURP: 53	3.7 (1.7–5.7)[a]	3.6 (1.7–5.5)[a]	NS	NA	NA	NA
Insausti et al, 2020[16]	PAE: 23 TURP: 22	3.5 (2.4–4.7)[a]	4.4 (0.8–8.0)[a]	NR	NA	NA	NA
3 Months							
Abt et al, 2018[14]	PAE: 48 TURP: 51	2.3 (Not estimable)	1.2 (Not estimable)	.07	−1.9 (−2.7 to −1.0)[b]	−3.2 (−4.0 to −2.3)[b]	NR
Gao et al, 2014[13]	PAE: 54 TURP: 53	2.2 (1.3–3.1)[a]	1.5 (0.7–2.3)[a]	.001	−1.5 (−3.7 to 0.7)[b]	−2.1 (−4.2 to 0.0)[b]	NR
Insausti et al, 2020[16]	PAE: 23 TURP: 22	1.9 (1.3–2.6)[a]	0.9 (0.6–1.3)[a]	NR	−1.6 (−2.9 to −0.3)[b]	−3.4 (−7.1 to 0.2)[b]	NR
6 Months							
Gao et al, 2014[13]	PAE: 57 TURP: 57	2.0 (1.2–2.8)[a]	1.7 (1.0–2.4)[a]	NS	−1.7 (−3.9 to 0.5)[b]	−1.9 (−3.9 to 0.1)[b]	NR
12 Months							
Carnevale et al, 2016[39]	Original PAE: 15 PErFecTED PAE: 15 TURP: 15	Original: 2.2 (1.6–2.8) PErFecTED: 1.7 (1.1–2.3)	1.6 (1.1–2.1)	NS	Original: −1.2 (−2.4 to 0.0)[b] PErFecTED: −2.0 (−3.2 to −0.8)[b]	−1.6 (−2.9 to −0.3)[b]	NR
Gao et al, 2014[13]	PAE: 54 TURP: 53	2.1 (1.2–3.0)[a]	1.6 (0.8–2.4)[a]	.009	−1.6 (−3.8 to 0.6)[b]	−2.0 (−4.1 to 0.1)[b]	NR
Insausti et al, 2020[16]	PAE: 23 TURP: 22	2.8 (2.0–3.7)[a]	1.7 (0.9–2.4)[a]	.013	−0.7 (−2.1 to 0.7)[b]	−2.7 (−6.4 to 1.0)[b]	.013
24 Months							
Gao et al, 2014[13]	PAE: 47 TURP: 48	2.1 (1.4–2.8)[a]	1.7 (0.9–2.5)[a]	.012	−1.6 (−3.9 to 0.7)[b]	−1.9 (−4.0 to 0.2)[b]	NR

Abbreviations: CI, confidence interval; NA, not applicable; NR, not reported; NS, not significant; PAE, prostatic artery embolization; PSA, prostate-specific antigen; TURP, transurethral resection of the prostate.

[a]Estimated 95% confidence intervals were extracted from graphs using WebPlotDigitizer.[34]

[b]Change from baseline was calculated and the corresponding standard deviation was imputed.

PROSTATIC ARTERY EMBOLIZATION VERSUS OPEN SIMPLE PROSTATECTOMY
Mean PSA levels were found to be significantly lower in the simple open prostatectomy group at 6 months and at 1 year compared with PAE (Table 14).[17]

We rated the quality of the evidence for PSA levels at 6 and 12 months as very low, downgrading for risk of bias, indirectness, and imprecision (see Appendix 4, Table A5).

Table 14: Prostate-Specific Antigen Levels for Prostatic Artery Embolization Versus Open Simple Prostatectomy

		Mean PSA, ng/mL (95% CI)			Mean PSA Change From Baseline, ng/mL (95% CI)		
Study	**N**	**PAE**	**OSP**	***P* Value**	**PAE**	**OSP**	***P* Value**
Baseline							
Russo et al, 2015[17]	PAE: 80 OSP: 80	3.6 (3.2–4.0)	4.2 (3.8–4.6)	.1	NA	NA	NA
6 Months							
Russo et al, 2015[17]	PAE: 80 OSP: 80	2.4 (2.2–2.6)	1.4 (0.9–1.9)	< .01	−1.2 (−1.6 to −0.7)[a]	−2.8 (−3.4 to −2.1)[a]	NR
12 Months							
Russo et al, 2015[17]	PAE: 80 OSP: 80	2.1 (1.9–2.3)	1.3 (1.0–1.7)	< .01	−1.5 (−1.9 to −1.0)[a]	−2.9 (−3.4 to −2.3)[a]	NR

Abbreviations: CI, confidence interval; NA, not applicable; NR, not reported; OSP, open simple prostatectomy; PAE, prostatic artery embolization; PSA, prostate-specific antigen.
[a]Change from baseline was calculated and the corresponding standard deviation was imputed.

Clinical and Technical Failure Rate

PROSTATIC ARTERY EMBOLIZATION VERSUS TRANSURETHRAL RESECTION OF THE PROSTATE
Two studies[13,39] reported on the clinical and technical failure rate of PAE compared with TURP, using different definitions (Table 15). Clinical success or failure for PAE was defined as a composite measure, as a combination of either IPSS, quality of life, or peak urinary flow rate. The clinical failure rate of PAE ranged from 0% to 13.3%, compared with 0% to 3.8% for TURP.

Technical success or failure for PAE was also variably defined, either as unilateral or bilateral embolization. The technical failure rate of PAE ranged from 0% to 13.3%. Carnevale et al[39] did not use a standard urology definition for clinical success for BPH. The authors found clinical and technical failure rates of 13.3% (2/15) for original PAE, compared with 0% (0/15) for the original PAE approach, but the results were limited to 15 participants in each group.[39]

Carnevale et al[39] found no recurrence of lower urinary tract symptoms in the PErFecTED PAE and TURP groups; however, two people (13.3%) in the original PAE group did experience recurrence (one at 6 months and another at 12). Both were treated with TURP to relieve symptoms.

Ray et al[15] did not explicitly report the definitions used or rates found for clinical and technical failure, but they did note that 43 people (19.9%) in the PAE group required reoperation (11 people [5.1%] within

12 months, and 32 people [14.8%] after 12 months). In the TURP group, five people (5.6%) required reoperation (3 people [3.4%] within 12 months, and 1 person [1.1%] after 12 months).

Table 15: Clinical and Technical Failure Rates for Prostatic Artery Embolization Versus Transurethral Resection of the Prostate

Study	Definition	Failure Rate
Carnevale et al, 2016[39]	Clinical success: IPSS ≤ 8 and/or QoL ≤ 3 at 12 mo	Original PAE: 2/15 (13.3%) PErFecTED: 0/15 (0%) TURP: 0/15 (0%)
	Technical success: bilateral embolization	Original PAE: 2/15 (13.3%) due to severe atherosclerosis or occlusion of the inferior vesical artery on one side PErFecTED: 0/15 (0%)
Gao et al, 2014[13]	Clinical failure: persisting severe symptoms (IPSS decrease of ≤ 25%, IPSS ≥ 18, QOL score decrease ≤ 1, and QOL score ≥ 4) and/or Q_{max} increase < 2.5 mL and Q_{max} ≤ 7 mL/s	PAE: 5/54 (9.3%) • Bilateral PAE: 4/48 (8.3%) • Unilateral PAE: 1/6 (16.7%) TURP: 2/53 (3.8%)
	Technical success: selective prostatic arterial catheterization and embolization on at least one side of the pelvis	PAE: 3/57 (5.3%) due to tortuosity and atherosclerotic changes in bilateral iliac arteries TURP: 0/57 (0%)

Abbreviations: IPSS, Internal Prostate Symptom Score; PAE, prostatic artery embolization; PErFecTED, proximal embolization first then embolize distal method of prostatic artery embolization; Q_{max}, peak (maximum) urinary flow; QOL, quality of life; TURP, transurethral resection of the prostate.

PROSTATIC ARTERY EMBOLIZATION VERSUS OPEN SIMPLE PROSTATECTOMY

Russo et al[17] noted that the technical success of PAE was determined by selective angiography performed after the procedure but did not report on the clinical or technical failure rate of PAE compared with OSP.

Patient Satisfaction

PROSTATIC ARTERY EMBOLIZATION VERSUS TRANSURETHRAL RESECTION OF THE PROSTATE

Insausti et al[16] was the only study reporting on patient satisfaction for PAE compared with TURP (Table 16). The authors developed and used a 100-point scale (from 0, “very dissatisfied,” to 100, “very satisfied”). At discharge and at 1 month, the PAE group had significantly higher satisfaction scores than the TURP group.

Table 16: Patient Satisfaction for Prostatic Artery Embolization Versus Transurethral Resection of the Prostate

Study	Time	PAE Mean (SD)	TURP Mean (SD)	*P* Value
Insausti et al, 2020[16]	Discharge	88.3 (17.2)	75.0 (12.6)	.005
	1 mo	88.9 (16.5)	65.9 (16.2)	< .001

Abbreviations: PAE, prostatic artery embolization; SD, standard deviation; TURP, transurethral resection of the prostate.

PROSTATIC ARTERY EMBOLIZATION VERSUS OPEN SIMPLE PROSTATECTOMY

No studies were found reporting on patient satisfaction for PAE compared with OSP.

Adverse Events

PROSTATIC ARTERY EMBOLIZATION VERSUS TRANSURETHRAL RESECTION OF THE PROSTATE

Table 17 presents the adverse events reported in studies comparing PAE with TURP. The most common adverse events were hematuria, urinary infection, and urinary retention. Some studies reported adverse events that occurred only in the TURP group (e.g., bladder neck stenosis, bladder or urethral strictures, and TUR syndrome), likely due to the more invasive nature of TURP. In addition, in almost all of the studies, incontinence, ejaculation disorders (e.g., reduction in ejaculation volume or retrograde ejaculation [where semen is ejaculated backward into the bladder rather than out through the penis]), and erectile dysfunction were higher in the TURP group than in the PAE group. The small participant numbers within many of the studies make it difficult to assess whether these differences were statistically significant. No deaths were reported in any of the studies.

Adverse events were defined using the Clavien classification system, which ranges from grade 1 (any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions) to grade 4 (death).[43] Major adverse events (Clavien grade ≥ 3, defined as complications requiring at least surgical, endoscopic, or radiological intervention[43]) were rare in the PAE group (with many reporting zero cases), compared with the TURP group. The highest reported adverse events that were Clavien grade ≥ 3 occurred in the study by Gao et al,[13] but these numbers also included clinical and technical failures, unlike other studies. Gao et al[13] reported that 8 of 54 (14.8%) people in the PAE group experienced major adverse events; all of them due to clinical or technical failure. Within the TURP group, 4 of 53 (7.5%) participants experienced major adverse events, which included two technical failures and one case each of TUR syndrome and bladder neck stenosis. Carnevale et al[39] found that the PErFecTED PAE approach had fewer adverse events than the original PAE approach, but only 15 participants were included in each group.

No studies assessed the long-term impact of radiation exposure from PAE.

Table 17: Adverse Events for Prostatic Artery Embolization Versus Transurethral Resection of the Prostate

Adverse Event	Abt et al, 2018[14]		Carnevale et al, 2016[39]			Gao et al, 2014[13]		Insausti et al, 2020[16]		Ray et al, 2018[15]	
	PAE n (%)	TURP n (%)	Original PAE n (%)	PErFecTED PAE n (%)	TURP n (%)	PAE n (%)	TURP n (%)	PAE n (%)	TURP n (%)	PAE n (%)	TURP n (%)
Clavien grade ≥ 3	2/48 (4.2%)	7/51 (13.7%)	0/15 (0%)	0/15 (0%)	2/15 (13.3%)	8/54 (14.8%)	4/53 (7.5%)	0/23 (0%)	1/22 (4.5%)	NR	NR
Bladder neck stenosis	NR	NR	NR	NR	NR	0/47 (0%)	1/48 (2.1%)	NR	NR	NR	NR
Bladder or urethral stricture	0/48 (0%)	2/51 (3.9%)	NR	NR	NR	0/47 (0%)	1/48 (2.1%)	0/23 (0%)	2/22 (9.1%)	NR	NR
Blood transfusion	NR	NR	NR	NR	NR	0/54 (0%)	2/53 (3.8%)	NR	NR	NR	NR
Clot retention	NR	NR	NR	NR	NR	0/54 (0%)	1/53 (1.9%)	NR	NR	NR	NR
Hematospermia	NR	NR	1/15 (6.7%)	1/15 (6.7%)	NR	NR	NR	NR	NR	25/199 (12.6%)	1/61 (1.6%)
Hematuria	4/48 (8.3%)	11/51 (21.6%)	2/15 (13.3%)	0/15 (0%)	15/15 (100%)	0/54 (0%)	4/53 (7.5%)	1/23 (4.3%)	8/22 (36.4%)	37/199 (18.6%)	39/61 (63.9%)
Ejaculation disorders	14/48 (29.2%)	21/51 (41.2%)	2/15 (13.3%)	1/15 (6.7%)	15/15 (100%)	NR	NR	1/23 (4.3%)	9/22 (40.9%)	48/199 (24.1%)	29/61 (47.5%)
Erectile dysfunction	NR	NR	NR	NR	NR	NR	NR	1/23 (4.3%)	5/22 (22.7%)	NR	NR
Left venous sinus damage	NR	NR	0/15 (0%)	0/15 (0%)	1/15 (6.7%)	NR	NR	NR	NR	NR	NR
Rectal ischemia	NR	NR	NR	NR	NR	NR	NR	1/23 (4.3%)	0/22 (0%)	NR	NR
Transient rectal bleeding	NR	NR	1/15 (6.7%)	1/15 (6.7%)	0/15 (0%)	NR	NR	NR	NR	NR	NR
Transient pubic bone ischemia	NR	NR	1/15 (6.7%)	0/15 (0%)	0/15 (0%)	NR	NR	NR	NR	NR	NR
TUR syndrome	NR	NR	NR	NR	NR	0/54 (0%)	1/53 (1.9%)	NR	NR	NR	NR

Adverse Event	Abt et al, 2018[14]		Carnevale et al, 2016[39]			Gao et al, 2014[13]		Insausti et al, 2020[16]		Ray et al, 2018[15]	
	PAE n (%)	TURP n (%)	Original PAE n (%)	PErFecTED PAE n (%)	TURP n (%)	PAE n (%)	TURP n (%)	PAE n (%)	TURP n (%)	PAE n (%)	TURP n (%)
Urinary incontinence	0/48 (0%)	3/51 (5.9%)	NR	NR	4/15 (26.7%)	NR	NR	0/23 (0%)	3/22 (13.6%)	2/199 (1.0%)	2/61 (3.3%)
Urinary infection	10/48 (20.8%)	19/51 (37.3%)	NR	NR	NR	1/54 (1.9%)	2/53 (3.8%)	0/23 (0%)	4/22 (18.2%)	10/199 (5.0%)	1/61 (1.6%)
Urinary retention	1/48 (2.1%)	3/51 (5.9%)	NR	NR	NR	14/54 (25.9%)	3/53 (5.7%)	5/23 (21.7%)	4/22 (18.2%)	NR	NR
Other	6/48 (12.5%)	7/51 (13.7%)	NR	NR	NR	22/54 (40.7%)	13/53 (24.5%)	NR	NR	NR	NR

Abbreviations: NR, not reported; PAE, prostatic artery embolization; PErFecTED, proximal embolization first then embolize distal method of PAE; TUR, transurethral resection; TURP, TUR of the prostate.

PROSTATIC ARTERY EMBOLIZATION VERSUS OPEN SIMPLE PROSTATECTOMY

Compared with OSP, Russo et al[17] found that PAE was associated with fewer adverse events (all grades) than OSP (17.5% vs. 60.0%), and also Clavien grade 1 (any deviation from the normal postoperative course) and grade 2 (normal course altered) complications ($P < .05$).[17,43] The most common adverse events for PAE were grade 1 (7.5%), which included hematospermia, fever, pain, wound discharge, anastomotic leakage (leakage from a surgical join), and stress incontinence. Compared with PAE, OSP resulted in similar numbers of Clavien grade 1 and 2 complications (13.8% and 12.5%). No Clavien grade 3a complications (complications that require an intervention performed under local anesthesia[43]) were found in the PAE group, but 3 of 80 (12.5%) were noted for the OSP group. No participants in either group required re-catheterization or reoperation. The long-term impact of radiation exposure from PAE was not assessed.

Table 18: Adverse Events of for Prostatic Artery Embolization Versus Open Simple Prostatectomy

	Russo et al, 2015[17]	
Adverse Event	**PAE, n (%)**	**OSP, n (%)**
Clavien grade 1	6/80 (7.5%)	11/80 (13.8%)
Clavien grade 2	1/80 (1.3%)	10/80 (12.5%)
Clavien grade 3a	0/80 (0%)	3/80 (3.8%)
Anemia	0/80 (0%)	5/80 (6.3%)
Hematospermia	1/80 (1.3%)	0/80 (0%)
Hematuria	0/80 (0%)	4/80 (5.0%)
Incontinence	0/80 (0%)	3/80 (3.8%)
Stricture	0/80 (0%)	2/80 (2.5%)
Urinary infection	1/80 (1.3%)	3/80 (3.8%)
Other	5/80 (6.3%)	7/80 (8.8%)

Abbreviations: OSP, open simple prostatectomy; PAE, prostatic artery embolization.

Ongoing Studies

We are aware of four ongoing clinical comparative studies on PAE (Table 19). The included study by Abt et al[14] is estimated to be completed in December, 2022 (interim 12-week data are currently available). We found another ongoing study comparing PAE with TURP or open prostatectomy[44] and one study comparing PAE with standard combined drug therapy (alpha blockers and 5-alpha-reductase inhibitors).[45] The Cantonal Hospital St. Gallen in Switzerland is also conducting an ongoing registry study to evaluate the efficacy and safety of BPH treatments, which includes PAE.[46]

Table 19: Ongoing Comparative Clinical Studies on Prostatic Artery Embolization

ClinicalTrials.gov Trial Number	Title	Sponsor, Country	Study Design	Comparator	Estimated Completion Date
NCT02869971	PAE vs. medical treatment in symptomatic BPH	Assistance Publique - Hôpitaux de Paris, France	RCT	Standard combined drug therapy (alpha blockers and 5-alpha-reductase inhibitors)	March 2022
NCT02054013	PAE vs. conventional transurethral prostatectomy in the treatment of BPH: a prospective randomized trial	Daniel Stephan Engeler, Switzerland	RCT	Monopolar TURP	December 2022
NCT04084938	PAE vs. TURP or OP in patients with symptomatic BPH	Oslo University Hospital, Norway	RCT	TURP or OP	December 2027
NCT03521648	Database for the assessment of efficacy and safety of BPH treatment	Dominik Abt, Switzerland	Observational registry study	Other surgical procedures for BPH (e.g., TURP, OP, HoLEP, TUIP, thulium laser vaporization, resection, or enucleation)	December 2027

Abbreviations: BPH, benign prostatic hyperplasia; HoLEP, holmium laser enucleation of the prostate; OP, open prostatectomy; PAE, prostatic artery embolization; RCT, randomized controlled trial; TUIP, transurethral incision of the prostate; TURP, transurethral resection of the prostate.

Discussion

We found limited comparative evidence for the effectiveness for PAE and other treatments for BPH. The only comparators found for PAE were TURP and OSP. Transurethral resection of the prostate is the standard procedure for BPH; OSP is not commonly performed in Ontario and is primarily reserved for people with very large prostates.

Our results generally align with previous systematic reviews (Appendix 2). In general, we found significant improvements in outcomes for both PAE and TURP. Some studies noted a significant improvement in outcomes favouring TURP in the short term (3 months) that did not persist at 1 year or later (e.g., prostate volume, peak urinary flow, post-void residual volume).[13,14] The authors noted that this is likely explained by the slower symptom improvements of PAE compared with TURP. In other studies, the outcome results sometimes slightly favoured PAE or the comparator (TURP or OSP); however, the differences were not statistically significant between groups.

In general, PAE may improve BPH symptoms and urodynamic measures, but we are uncertain if PAE results in outcomes similar to those of TURP. One small study indicated that PAE may result in less erectile dysfunction compared with TURP, but we are very uncertain of the evidence.[39] Only one study evaluated patient satisfaction, which showed greater satisfaction among the PAE group at discharge and 1 month compared with TURP.[16]

Based on one nonrandomized study, OSP showed significantly greater improvement in IPSS, health-related quality of life, peak urinary flow rate, post-void residual volume, and PSA levels at 1 year,

compared with PAE.[17] In contrast, PAE may result in less erectile dysfunction compared with OSP, but we are very uncertain about the evidence.

Clinical outcomes were assessed using standardized or validated tools, which reduced measurement variability. All studies measured erectile function using the IIEF (either the shortened five- or six-question version) and assessed quality of life using the IPSS–Quality of Life scale. However, clinical and technical success or failure was variably defined within the studies and did not always reflect standard clinical definitions.

There were considerable risk-of-bias concerns among the included studies. Randomization was often unclear in the RCTs, and differences in baseline characteristics in studies were not always adjusted for, which affected study results. Three studies used noninferiority designs,[14-16] and at least two[16,39] were likely too underpowered to detect differences among study groups. Almost all studies were single-centre studies. For these reasons, we judged the overall generalizability of the included studies to be low.

Fewer adverse events were found for PAE compared with TURP or OSP. While many of the included studies had small sample sizes, this result aligns with the less invasive nature of the PAE procedure. There is also no risk of some adverse events in PAE as can be found with TURP, such as TUR syndrome, retrograde ejaculation, and bladder incontinence. Conversely, adverse events unique to PAE exist, but none were reported within the included studies (e.g., femoral artery puncture site pseudoaneurysm and contrast-induced nephropathy). Noncomparative studies have also shown similarly low adverse event rates for PAE.[47] However, the long-term safety of PAE is unclear.

We did not find any long-term comparative data for PAE. There is also a lack of large longer-term cohort studies on PAE. Only one study, by Gao et al,[13] evaluated PAE and TURP at 2 years, while all the other studies had follow-up durations of 1 year or less. The longer-term direct comparative effectiveness of the two procedures is, therefore, unclear. However, according to longer-term noncomparative studies, the positive effect of PAE on functional outcomes such as IPSS and quality of life may still be maintained up to 6.5 years, with no urinary incontinence or sexual dysfunction.[47] Clinical success rates of about 76% have been reported for timeframes of up to 6.5 years.[47]

While there is limited comparative evidence for PAE, the procedure provides an alternative for people with moderate to severe BPH who may have failed medical therapy and who cannot or choose not to have surgical treatment. Ongoing studies will also provide further evidence for the effectiveness and safety of PAE compared with BPH treatment options. Future longer-term studies are needed to compare PAE with other available surgical and minimally invasive treatment options for BPH.

Strengths and Limitations

We have included the most recent evidence on the effectiveness and safety of PAE compared with other treatment options for PAE. While numerous systematic reviews (Appendix 2) have been published for PAE, they differed in their population, comparator, outcomes of interest, and methods, and study results were not consistently analyzed within the reviews. Some of the previously conducted systematic reviews meta-analyzed outcomes despite the presence of considerable statistical heterogeneity or they combined different study designs, time points, or comparators in their analyses. We chose not to conduct a meta-analysis due to these population and study methodology differences.

Our results are limited by the reporting of the included studies. Three studies[13,14,16] did not explicitly report 95% confidence intervals for all our relevant outcomes of interest at all time points. In these cases, we estimated values from graphs using software, where available. Most studies did not report the variance associated with outcome changes from baseline. In these cases, we imputed standard deviations for comparisons between studies. We used a conservative formula to impute these standard deviations (assuming a correlation coefficient of 1), but this leads to lower precision (wider confidence intervals) in our estimates. We were not able to assess the impact of the PAE approach or particle size as originally planned due to the limited number of studies. Some studies have shown that particle size may impact the functional outcomes of PAE.[8-11]

Conclusions

We found limited comparative evidence on the effectiveness and safety of PAE for BPH, especially in the long term (beyond 1 year). We only found studies comparing PAE with TURP or OSP. The included studies were affected by considerable risk-of-bias concerns and had different participant populations and study methodologies.

Prostate artery embolization may improve BPH symptoms and urodynamic measures, but we are uncertain if PAE results in similar outcomes to those of TURP (GRADE: Very low to Low). Compared with TURP, PAE may result in higher patient satisfaction and fewer adverse events (GRADE: Not assessed).

Compared with OSP, PAE may result in smaller improvement in BPH symptoms and urodynamic measures and fewer adverse events, but the evidence is very uncertain (GRADE: Very low).

Economic Evidence

Research Question

What is the cost-effectiveness of prostatic artery embolization (PAE) compared with surgical and minimally invasive procedures for the treatment of people with benign prostatic hyperplasia (BPH)?

Methods

Economic Literature Search

We performed an economic literature search on November 22, 2019, to retrieve studies published from database inception until the search date. To retrieve relevant studies, we developed a search using the clinical search strategy with an economic and costing filter applied.

We created database auto-alerts in MEDLINE and Embase and monitored them for the duration of the assessment period. We also performed a targeted grey literature search of health technology assessment agency websites, clinical trial and systematic review registries, and the Tufts Cost-Effectiveness Analysis Registry. The grey literature search was updated on August 14, 2020. See Clinical Literature Search, above, for further details on methods used. See Appendix 3 for our literature search strategies, including all search terms.

Eligibility Criteria

STUDIES

Inclusion Criteria

- English-language full-text publications
- Cost-benefit analyses, cost-effectiveness analyses, cost-minimization analyses, cost-consequence analyses, or cost–utility analyses

Exclusion Criteria

- Abstracts, case reports, editorials, commentaries, reviews, letters, unpublished studies
- Costing analyses

POPULATION

- People of any age with BPH

INTERVENTIONS

- Prostatic artery embolization using any type of embolic particles, via the femoral or radial artery and using any type of embolization approach (e.g., unilateral or bilateral)

OUTCOME MEASURES

- Costs
- Health outcomes (e.g., quality-adjusted life-years [QALYs])

- Incremental costs and incremental effectiveness
- Incremental cost-effectiveness ratios (ICER)

Literature Screening

A single reviewer conducted an initial screening of titles and abstracts using Covidence[48] and then obtained the full texts of studies that appeared eligible for review according to the inclusion criteria. The same reviewer then examined the full-text articles and selected studies eligible for inclusion.

Data Extraction

If an eligible study were identified, we would have extracted relevant data on study characteristics and outcomes to collect information about the following:

- Source (e.g., citation information, study type)
- Methods (e.g., study design, analytic technique, perspective, time horizon, population, intervention, comparators)
- Outcomes (e.g., health outcomes, costs, incremental cost-effectiveness ratios)

Study Applicability and Limitations

If an eligible study were identified, we would have determined the usefulness of each study for decision-making by applying a modified quality appraisal checklist for economic evaluations originally developed by the National Institute for Health and Care Excellence (NICE) in the United Kingdom to inform the development of NICE's clinical guidelines.[49] We modified the wording of the questions to remove references to guidelines and to make it specific to Ontario. Next, we separated the checklist into two sections. In the first section, we assessed the applicability of each study to the research question (directly, partially, or not applicable). In the second section, we assessed the limitations (minor, potentially serious, or very serious) of the studies that we found to be directly applicable.

Results

Economic Literature Search

The database search of the economic literature search yielded 29 citations published from database inception until November 22, 2019. We identified six additional studies from other sources, for a total of 28 after removing duplicates. We did not identify any studies that met our inclusion criteria. See Appendix 5 for a list of studies excluded after full-text review. Figure 2 presents the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram for the economic literature search.

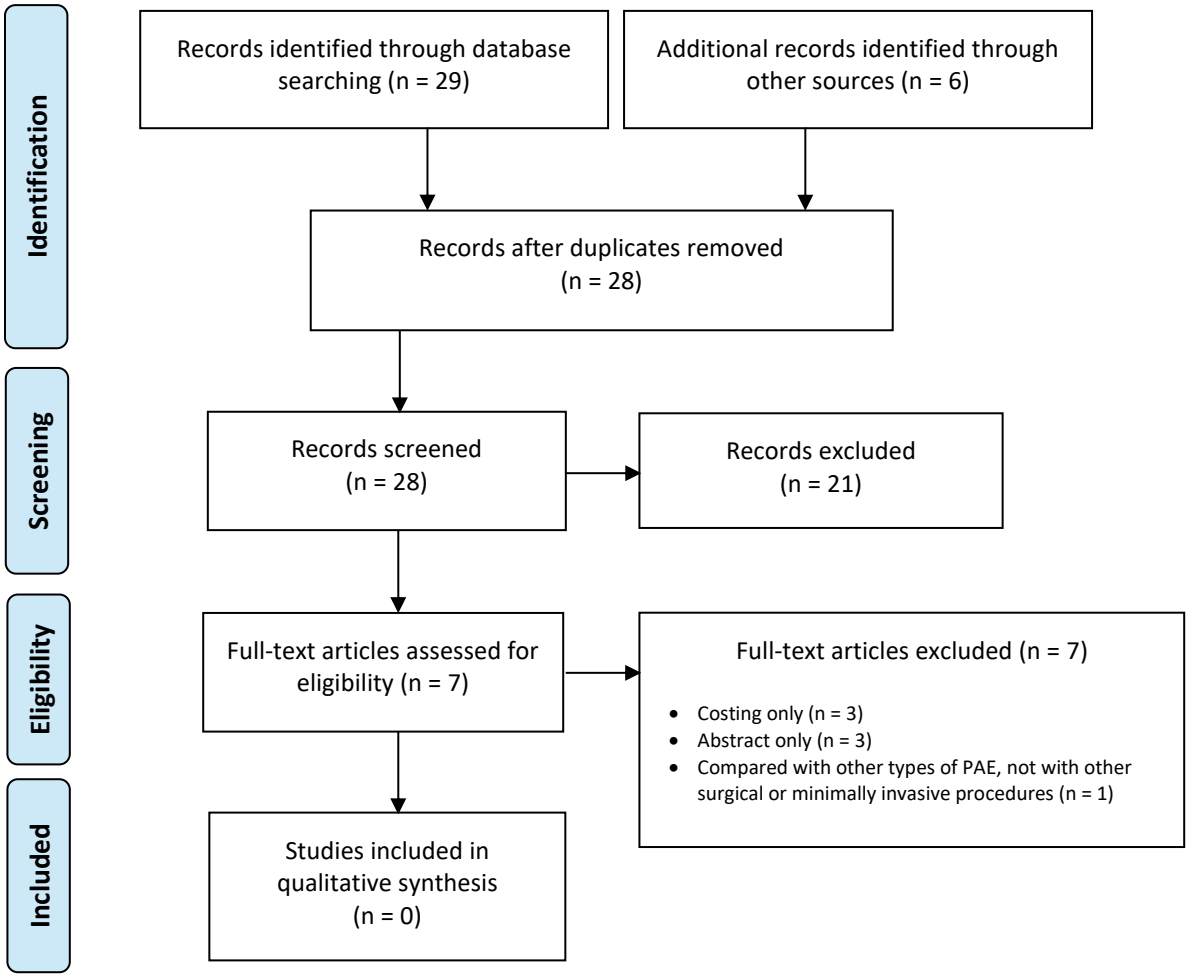

Figure 2: PRISMA Flow Diagram—Economic Search Strategy

Abbreviation: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses.
Source: Adapted from Moher et al.[50]

Discussion

Although we did not identify any published cost-effectiveness studies, we found three costing analyses comparing PAE with alternative therapies,[31,51,52] one of which was conducted in Ontario[31] (see detailed results in Appendix 6).

Bagla et al[51] compared direct costs of elective PAE and TURP in a hospital setting in the United States by reviewing patient charts and hospital financial data retrospectively. A total of 70 PAE patients and 86 TURP patients were included. The study included direct costs such as nursing and operating room or interventional room staffing, operating room or interventional supplies, anaesthesia, anaesthesia staffing, hospital room, radiology, and laboratory. It did not include indirect hospital costs such as electricity, housekeeping, security, medical records, or pathology. Professional physician fees of the anaesthesiologist, radiologist, and urologist were also not included. The authors found that there was a significant difference in the average age of patients undergoing PAE and TURP (64.4 vs. 71.3 years, $P < 0.0001$). The cost of intra-procedural supplies for PAE were significantly greater than those of TURP ($1,472.77 vs. $1,080.84, $P < 0.0001$ [2014 USD]). When including anaesthesia supplies and nursing/staffing, the PAE procedure was less costly than TURP ($1,667.10 vs. $2,153.64, $P < 0.0001$). The average length of stay for PAE patients was shorter than for TURP patients (0.125 vs. 1.38 days). Total in-patient costs for the PAE group ($1,678.14, SD $442.0) was significantly lower than for the TURP group ($5,338.31, SD $3,521.17, $P < 0.0001$).

Brown et al[31] conducted a retrospective chart review of patients who underwent PAE, TURP, and photoselective vaporization (PVP) from April, 2015, to March, 2017, in an Ontario hospital. The study included a total of 21 PAE patients, 209 TURP patients, and 28 PVP patients. All hospital costs were collected in accordance with the Ontario Case Costing Initiative, a standardized medical case costing system. The analysis considered costs incurred from the time of admission to subsequent discharge as well as costs related to any re-admissions within 30 days of the procedure. Both direct and indirect costs were included. Direct costs were those related to patient-specific services such as nursing care, laboratory interventions, and imaging exams. Indirect costs included administrative services, finance, and housekeeping. Physician fees were excluded from the analysis as they are not borne by the hospital. The study found that the average age of patients was similar between groups: PAE: 70.8; TURP: 71.4; PVP: 73.7 ($P = 0.366$). The average length of stay for PAE, TURP, and PVP was 1, 1.63, and 1.55 days, respectively ($P = 0.076$). Total cost of PAE, TURP, and PVP was $3,868, $4,101, and $4,622 (2017 USD), respectively.[31] Although PAE had higher intra-operative costs (i.e., interventional radiology consumables and angiography suite costs), its overall cost was lower because it did not require general anaesthesia and had lower post-operative costs.

Mullhaupt et al[52] perform a *post hoc* analysis of in-hospital costs incurred in a randomized controlled trial comparing PAE and TURP in Switzerland (Abt et al, 2018[53]). Costs were calculated using detailed expenditure reports provided by the hospital. Total costs, including those arising from surgical and interventional procedures, consumables, personnel, and accommodations, were analysed for all study participants and compared between the PAE and TURP groups. The mean total costs per patient were higher for TURP (€9,137 ± 3,301) than for PAE (€8,185 ± 1,630), although the mean difference of €952 was not statistically significant ($P =0.07$). While the mean procedural costs were significantly higher for PAE (mean difference €623; $P = 0.009$), costs apart from the procedure were significantly lower for PAE, with a mean difference of €1,627 ($P < 0.001$). Procedural costs of €1,433 ± 552 for TURP were mainly incurred by anaesthesia, whereas €2,590 ± 628 for medical supplies were the main cost factor for PAE. All costs were provided in 2017 EUR.

Although these three studies included different cost components and were conducted in different countries, all found PAE to be less costly than TURP. However, none of the studies considered long-term costs related to post-operative adverse events and potential re-intervention. Also, two studies did not include costs related to physician fees.[31,51] Lastly, some studies are limited by a relatively small sample size of PAE patients.

Conclusions

Overall, the economic evidence on PAE is limited. We did not identify any cost-effectiveness studies comparing PAE with alternative treatments for BPH. We did, however, identify three costing studies (including one in Ontario) that showed PAE to be less costly than TURP from the hospital perspective.

Primary Economic Evaluation

Although we did not find any published cost-effectiveness studies comparing prostatic artery embolization (PAE) with alternative treatments for benign prostatic hyperplasia (BPH), we found several costing studies (including one Ontario study[31]) comparing PAE with transurethral resection of the prostate (TURP). These studies showed that PAE may be less expensive in the short term; however, they did not take into consideration physician fees and long-term costs related to adverse events and re-intervention. Our clinical evidence review showed that PAE may improve BPH symptoms and result in fewer adverse events, but the evidence is uncertain and it has higher clinical failure rates at 1- and 2-year follow-ups. Therefore, we decided to conduct a primary economic evaluation to evaluate the trade-off between the short- and long-term costs and benefits associated with different treatments.

Research Question

What is the cost-effectiveness of PAE compared with surgery for people with BPH?

Methods

The information presented in this report follows the reporting standards set out by the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement.[54]

Type of Analysis

We conducted a cost–utility analysis to determine the costs and quality-adjusted life-years (QALYs) associated with PAE and other BPH treatment alternatives. QALY is a commonly used summary measure that combines the gains in both quantity and quality of life (e.g., one QALY represents 1 year of perfect health). We chose this type of analysis because utility inputs are available for our target population and a generic outcome measure such as QALY allows decision-makers to make comparisons across different conditions and interventions. We reported the total costs and total QALYs for each treatment, and the incremental cost per QALY gained.

Target Population

Our target population is people with BPH. More specifically, since treatment for BPH is necessary only if symptoms become bothersome, we limited our target population to people with BPH who present with symptoms. The symptoms of BPH are referred to collectively as lower urinary tract symptoms. Our target population thus includes people who have moderate to severe symptoms, have previously failed medical therapy, and are considering PAE or other surgical or minimally invasive interventions.[13]

In the reference case, we based our target population's characteristics on Gao et al,[13] the randomized controlled trial on PAE with the longest follow-up (2 years) and largest sample size (N = 114). The cohort has a mean age of 67 ± 8 years and an average baseline International Prostate Symptom Score (IPSS) of 23 ± 6 (Table 20). The Canadian BPH population[55] has similar age demographics to those of participants in the Gao et al study.[13]

Perspective

We conducted this analysis from the perspective of the Ontario Ministry of Health.

Interventions

Various treatment options are available for BPH, including medication and surgical or minimally invasive procedures. Symptom severity, prostate volume, age, and comorbid conditions are considered when determining treatment.[56] Medications are typically recommended as the first-line treatment for BPH, and may include alpha-blockers (to relax bladder neck muscles and muscles fibres in the prostate for easier urination), 5-alpha-reductase inhibitors (to block hormones that promote prostate gland growth), muscle relaxant, or combination therapy.[56] If symptoms worsen, surgical or minimally invasive procedures are considered. Typically, these procedures remove the excess tissue or shrink the prostate gland. Transurethral resection of the prostate is the standard surgical procedure to treat BPH.[56] In this surgical procedure, excess prostate tissue is removed using a resectoscope inserted through the penis. The procedure typically takes less than 60 minutes and the average length of stay in the hospital is 1.6 days.[31,57] People with substantially enlarged prostates (> 100 mL) are not eligible for TURP. In these people, open simple prostatectomy (OSP) is the recommended surgical treatment. In OSP, excess tissue is removed through incisions typically made in the lower abdomen.[56] Open simple prostatectomy takes about 2 to 4 hours, and the average length of stay in the hospital is 2 to 4 days.[58] In addition to hospitalization, TURP and OSP both require the use of general anesthesia. Both procedures also have potential complications, including bleeding, retrograde ejaculation, urinary incontinence, erectile dysfunction, and urethral strictures.[59,60]

Prostatic artery embolization is an alternative endovascular procedure for treating BPH. It involves first inserting a catheter via the femoral artery (in the groin) or radial artery (in the wrist) under x-ray guidance. Contrast medium (x-ray dye) is injected through the catheter to map the flow of blood through the small arteries that supply the prostate gland; embolic particles are then injected to embolize the prostatic arteries, blocking the prostate gland's blood supply and causing it to undergo necrosis.[61] Symptoms may improve gradually over the course of a few months (up to 2 years).[13] The procedure is conducted by an interventional radiologist in a specialized angiography unit.[62] Prostatic artery embolization is performed using local anesthesia as a day procedure (average procedure time ranges from 90 to 150 minutes).[13-17] General anesthesia and hospitalization are not required for PAE. Prostatic artery embolization may be a less invasive option for BPH and an alternative to more invasive surgical treatments that carry potentially more serious complications (e.g., TURP).[57]

We compared PAE with alternative treatments for BPH. In our reference case, we compared PAE with TURP because TURP is the most common surgical treatment for BPH, and it is the only intervention that has been compared to PAE in published randomized controlled trials (RCTs).[13,16,53,63,64] In addition, to address the population that is not eligible for TURP (e.g., people with substantially enlarged prostates [> 100 mL]),[56] we compared PAE to OSP in a scenario analysis using clinical data from a comparative observational study.[65] There are no published clinical studies directly comparing PAE to other surgical or minimally invasive procedures (e.g., prostatic urethral lift or photoselective laser vaporization) or medications. Therefore, we did not include these treatment options in our evaluation.

Discounting and Time Horizon

In accordance with the Canadian Agency for Drugs and Technologies in Health (CADTH) guidelines,[66] we applied an annual discount rate of 1.5% to both costs and QALYs incurred after the first year. We used a cycle length of 3 months, similar to a previous Ontario microsimulation model by Erman et al,[67] which examined the cost-effectiveness of surgery (TURP and PVP) versus pharmacotherapy as the initial treatment for BPH. We used a time horizon of 6.5 years in the reference case. We chose this time horizon as it coincides with the longest follow-up of PAE in the clinical literature (i.e., in a non-

comparative study).[68] In a scenario analysis, we used a shorter time horizon of 2 years, which is the longest follow-up period in RCTs comparing TURP and PAE.[13] In addition, we used a longer time horizon of 10 years to examine potential long-term reintervention rates and symptom progression.

Model Structure

We developed a Markov microsimulation model to compare PAE and TURP and determine the incremental cost per QALY gained. We used a microsimulation model as it allowed us to reflect clinical pathways at an individual level, incorporate individuals' characteristics at baseline (e.g., age and IPSS scores), and capture the impact of past interventions on future trajectory more accurately.

We based our model structure and several inputs on an Ontario microsimulation model by Erman et al,[67] which compared surgery (e.g., TURP) to pharmacotherapy as the initial treatment for BPH. Our model structure is presented in Figure 3.

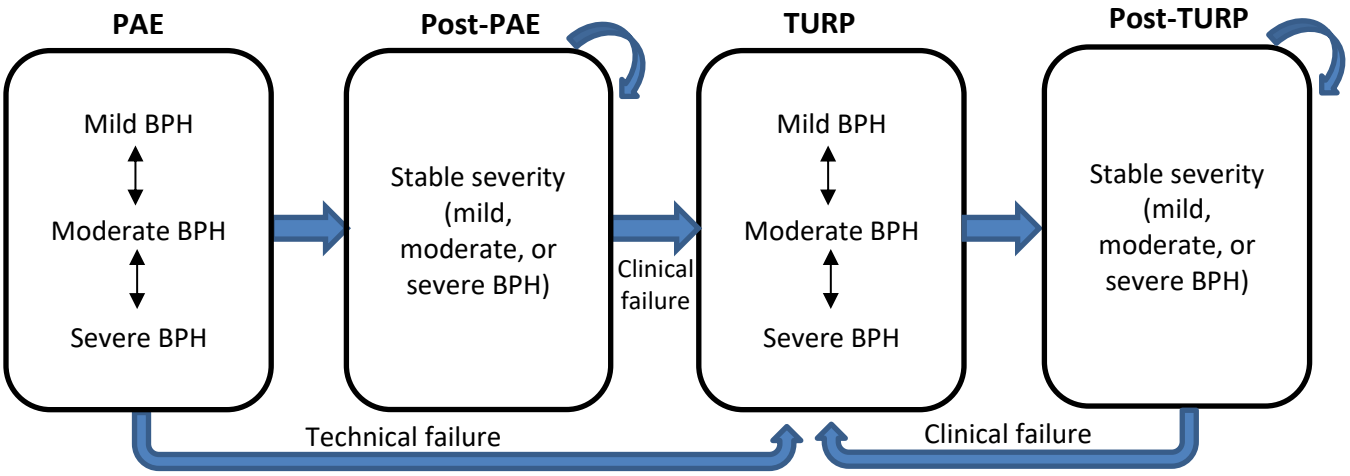

Figure 3: Model Structure

Abbreviations: BPH, benign prostatic hyperplasia; PAE, prostatic artery embolization; TURP, transurethral resection of the prostate.
Note: Individuals may enter the death state at any point.

The model consisted of the following health states: PAE, post-PAE, TURP, post-TURP, and death. Within each state, except death, the severity of BPH is captured using the IPSS, a validated questionnaire with scores ranging from 0 (least severe symptoms) to 35 (most severe symptoms). Throughout the model, the IPSS score may change based on symptom improvement due to treatment (indicated by a decrease in IPSS score) or symptom worsening due to BPH progression (increase in IPSS score). The IPSS score is categorized into three severity levels: mild (≤ 7), moderate (8–19), and severe (≥ 20).[69] The BPH severity levels impact patients' quality of life. People may transition between the three severity levels, which affects QALYs.

Each simulated individual entered the model receiving either PAE or TURP.

PAE

For those receiving PAE, a proportion of people may experience technical failure during the procedure, that is, experiencing failure to achieve embolization. Since TURP is the standard surgical procedure for treating BPH, we assumed individuals who experienced technical failure of PAE would receive a subsequent TURP in the next cycle.

People who experienced technical success during the procedure would remain in the PAE state for 2 years.[13] During this time, their IPSS score would gradually improve due to surgery. The improvement in IPSS score is a result of improvement in urinary symptoms and quality of life. At the end of 2 years, these individuals are assessed for clinical failure (i.e., insufficient improvement in urinary symptoms after treatment) based on the extent of their IPSS improvement. Those with unsatisfactory IPSS improvement (e.g., IPSS improvement is ≤ 25% from baseline and IPSS score ≥ 18)[13] were more likely to experience clinical failure. Those who experienced clinical failure would also receive TURP, similar to those who had a technical failure. For further details on the definition of clinical failure and how it was implemented in the model, refer to the Clinical Failure section under Clinical Outcomes and Utility Parameters, below.

POST-PAE

All individuals who experienced clinical success would transition into the post-PAE state. These individuals (with realized improvements in IPSS) were assumed to have stable IPSS for the remainder of the time horizon (6.5 years). However, once in the post-PAE state, they could still experience clinical failure in any cycle until the end of the time horizon. The probability of clinical failure depended on the extent of IPSS improvement experienced by each individual earlier in the PAE state (as described in more detail in Clinical Failure, under Clinical Outcomes and Utility Parameters, below). After every cycle, those who experienced clinical success would remain in the post-PAE state, whereas those who experienced clinical failure would receive TURP.

TURP

People receiving TURP (i.e., patients who started with TURP in the model as well as those who transitioned into TURP following a failed PAE) stayed in the TURP state for the first 2 years, similar to those in the PAE group. During this time, everyone would gradually experience IPSS improvement due to TURP (technical failure is defined as failure to embolize the prostatic artery and therefore is specific to PAE).

Clinical failure is assessed at the end of year 2, when people who experience clinical failure receive a second TURP. These patients remain in the TURP state and experience IPSS change for another 2 years before clinical failure is assessed again.

POST-TURP

Those who experienced clinical success would transition into the post-TURP state, where their improved IPSS would remain stable for the remainder of the time horizon. Similar to the post-PAE state, once people move into the post-TURP state, there is still a chance for clinical failure to occur in any cycle until the end of the time horizon. This probability of clinical failure was dependent on the extent of IPSS improvement experienced by each individual earlier in the TURP state. After every cycle, those who experience clinical success would remain in the post-TURP state, whereas those who experience clinical failure would receive a second TURP and transition back to the TURP state.

The small proportion of people experiencing clinical failure from their second TURP would still move to the post-TURP state, and their IPSS would progress based on the natural history. The IPSS for people experiencing clinical success in the post-TURP state would remain stable for the rest of the time horizon.

DEATH

At any point during the model time horizon, individuals may die from natural causes. To estimate deaths, we used the male age-specific background mortality from the Ontario life table.[70] All health states except for the TURP state has an equal risk of death; those in the TURP state have a one-time increased risk of perioperative death during surgery.[67]

Main Assumptions

The major assumptions for our reference case analysis are:

- All individuals are eligible to undergo PAE or TURP. To account for people who are not eligible for TURP (i.e., prostate volume > 100 mL), we conducted a scenario analysis in which people received OSP instead
- IPSS improvements after procedures are experienced gradually over 2 years, based on the primary clinical study,[13] where IPSS was reported at multiple time points
- People who experienced technical failure (PAE) or clinical failure (PAE or TURP) would follow up with TURP. However, we conducted a scenario analysis in which these patients would receive a second PAE instead of TURP
- Clinical failure is first assessed 2 years after the procedure.[13] Those who did not meet the IPSS criteria for clinical success, such as those with unsatisfactory IPSS improvement (e.g., IPSS improvement ≤ 25% from baseline) and poor overall IPSS (e.g., IPSS ≥ 18) are more likely to experience clinical failure
- People who experienced clinical success after PAE or TURP would have improved and stable IPSS for the remainder of the time horizon (6.5 years). In the reference case, we assumed PAE and TURP would have equal periods of stable IPSS
- An individual could undergo a maximum of two TURPs (plus one PAE if the individual started in the PAE group)
    - People starting in the TURP group would have one repeat TURP if the first TURP failed
    - People starting in the PAE group could have two TURPs after they failed PAE. People who failed both TURPs would stay in the post-TURP state with IPSS progressing (getting worse) based on natural history

Clinical Outcomes and Utility Parameters

INTERNATIONAL PROSTATE SYMPTOM SCORE

The starting IPSS and age distributions for the simulated cohort, as well as the natural progression of IPSS, and IPSS changes after PAE and TURP for our reference case are listed in Table 20.

The baseline characteristics and IPSS change due to treatments were obtained from our clinical evidence review. Based on the characteristics reported in Gao et al,[13] the RCT comparing PAE and TURP that has

the longest follow-up and largest sample size, we gave our simulated cohort a starting IPSS of 23.[13] Each simulated individual in the model is assigned a randomly sampled starting IPSS based on the distribution reported in Gao et al.[13]

We also used the IPSS change, which provided people's IPSS after PAE and TURP at multiple time points (i.e., baseline, 1, 3, 6, 12, and 24 months) over a period of 2 years.[13] We obtained the average IPSS reported at each time point and calculated the average change in IPSS from one time point to the next. We used a web plot digitizer[71] to extract the 95% confidence intervals around the IPSS scores reported at each time point and used these to estimate the standard deviation around each change in IPSS. We used the standard deviation to assign a distribution to each change in IPSS and, in our model, we randomly sampled these distributions for each individual. We converted IPSS changes into 3-month intervals (i.e., our cycle length), assuming that IPSS change is constant between the reported time points. We then modelled the individual's IPSS change from baseline over 2 years.

In a scenario analysis, we used another RCT by Carnevale et al[63] with a shorter follow-up duration and a smaller sample size comparing PAE to TURP as an alternative source of IPSS parameters. The parameters used for this scenario are presented in Appendix 7A.

Table 20: Clinical Parameters (Baseline Characteristics and IPSS Change) Used in the Economic Model—Reference Case

	Mean	Lower 95% CI[a]	Upper 95% CI[a]		Distribution	Source
Baseline Characteristics						
Starting age (years)	67.05	50.86	83.24		Normal	Gao et al, 2014[13]
Starting IPSS	22.95	11.48	34.42		Normal	Gao et al, 2014[13]
IPSS Change[b]				**IPSS Score**		
PAE					Normal	Gao et al, 2014[13]
0–3 mo	−8.70	−18.55	1.15	0 mo: 24.30		
3–6 mo	−2.80	−12.34	6.74	3 mo: 15.60		
6–12 mo	−1.90	−9.08	5.28	6 mo: 12.80		
12–24 mo	−2.20	−8.00	3.60	12 mo: 10.90		
Total reduction	−15.60			24 mo: 8.70		
TURP					Normal	Gao et al, 2014[13]
0–3 mo	−13.70	−21.41	−5.99	0 mo: 24.70		
3–6 mo	0.30	−6.42	7.02	3 mo: 11.00		
6–12 mo	−1.10	−7.66	5.46	6 mo: 11.30		
12–24 mo	−1.80	−7.82	4.22	12 mo: 10.20		
Total reduction	−16.30			24 mo: 8.40		
Natural progression (Annual)	0.18	−2.21	2.57		Normal	Jacobsen et al, 1996[72]

Abbreviations: CI, confidence interval; IPSS, International Prostate Symptom Score; PAE, prostatic artery embolization; TURP, transurethral resection of the prostate.

[a]IPSS change was applied as IPSS change per 3-month cycle. The 95% confidence interval was calculated using standard deviation to reflect individual-level variability, which was required in the microsimulation model.

[b]Treatment effect was converted to IPSS change per 3-month cycle.

TECHNICAL FAILURE

There is not a fixed definition of technical failure for PAE. For our reference case, we used the definition provided by Gao et al[13]: the failure to achieve embolization on at least one side of the pelvis (unilateral embolization). We obtained the rate of technical failure for PAE from the same study. People who experienced technical failure from PAE received TURP as per the study protocol.[13] Those who underwent TURP would not experience technical failure as technical failure was specific to PAE (technical failure was defined as failure to embolize the prostatic artery). The probabilities of technical and clinical failure are listed in Table 21.

CLINICAL FAILURE

Definition and Relation to IPSS

The exact criteria for clinical failure varies between studies, although it is generally defined as limited improvement in urinary symptoms and quality of life, failure to void spontaneously, and/or limited increase in peak urinary flow.[13,73] A combination of factors are considered, such as IPSS, quality of life

questionnaire score, peak urinary flow, and the need for other medical or follow-up surgical therapy.[13,63,68] Typically, there is an IPSS component in the definition (e.g., a decrease in IPSS of ≤ 25% from baseline and IPSS ≥ 18, based on Gao et al).[13] Since our model tracks individual's IPSS change and IPSS change is a part of the clinical failure criteria, instead of applying the same probability of clinical failure to everyone in our cohort, we used an IPSS threshold to more accurately determine which individuals would experience clinical failure. In other words, simulated individuals have different probabilities of clinical failure depending on whether they meet the IPSS threshold of the clinical failure criteria.

Applying IPSS to Model Clinical Failure: End of Year 2

In the reference case, clinical success is first assessed at 2 years post-treatment. We assumed that individuals did not experience clinical failure until after 2 years because IPSS improvement after treatment may fluctuate over this time. This time frame was also chosen due to the availability of clinical failure data reported by Gao et al[13] at the end of their 2-year study period, where those who had a clinical failure were followed up with TURP. As such, we used their probability of clinical failure to model the proportion of people who had clinical failure and reoperation.

Figure 4 presents the schematic on using IPSS failure threshold to model clinical failure. We applied the IPSS failure threshold outlined in Gao et al[13] (a decrease in IPSS of ≤ 25% from baseline and IPSS ≥ 18) to estimate the proportion of people who failed to achieve IPSS "success." We then compared this number to the proportion of people who experienced clinical failure in the Gao study (9.26% and 3.77% for PAE and TURP, respectively). If there was a higher proportion of IPSS "failure" than clinical failure, then we assumed all people who experienced clinical failure were from the IPSS failure group. We calibrated the percentage of people in the IPSS failure group that would clinically fail to match the reported proportion of clinical failure.

Conversely, if there was a lower proportion of IPSS failure than clinical failure, we assumed all individuals who have IPSS failure would experience clinical failure, plus a proportion of those meeting just one component of the IPSS thresholds (a decrease in IPSS of ≤ 25% from baseline IPSS or IPSS ≥ 18). Finally, we assumed that individuals who met neither component of the IPSS failure threshold were unlikely to experience clinical failure. This approach ensured that those having unsatisfactory IPSS were more likely to experience clinical failure, and the proportion of IPSS failure is calibrated to match the proportion of clinical failure reported in the literature. Ultimately our approach attempted to ensure that QALYs, which were estimated based on a person's IPSS, were more accurate and reflective of real-life observations.

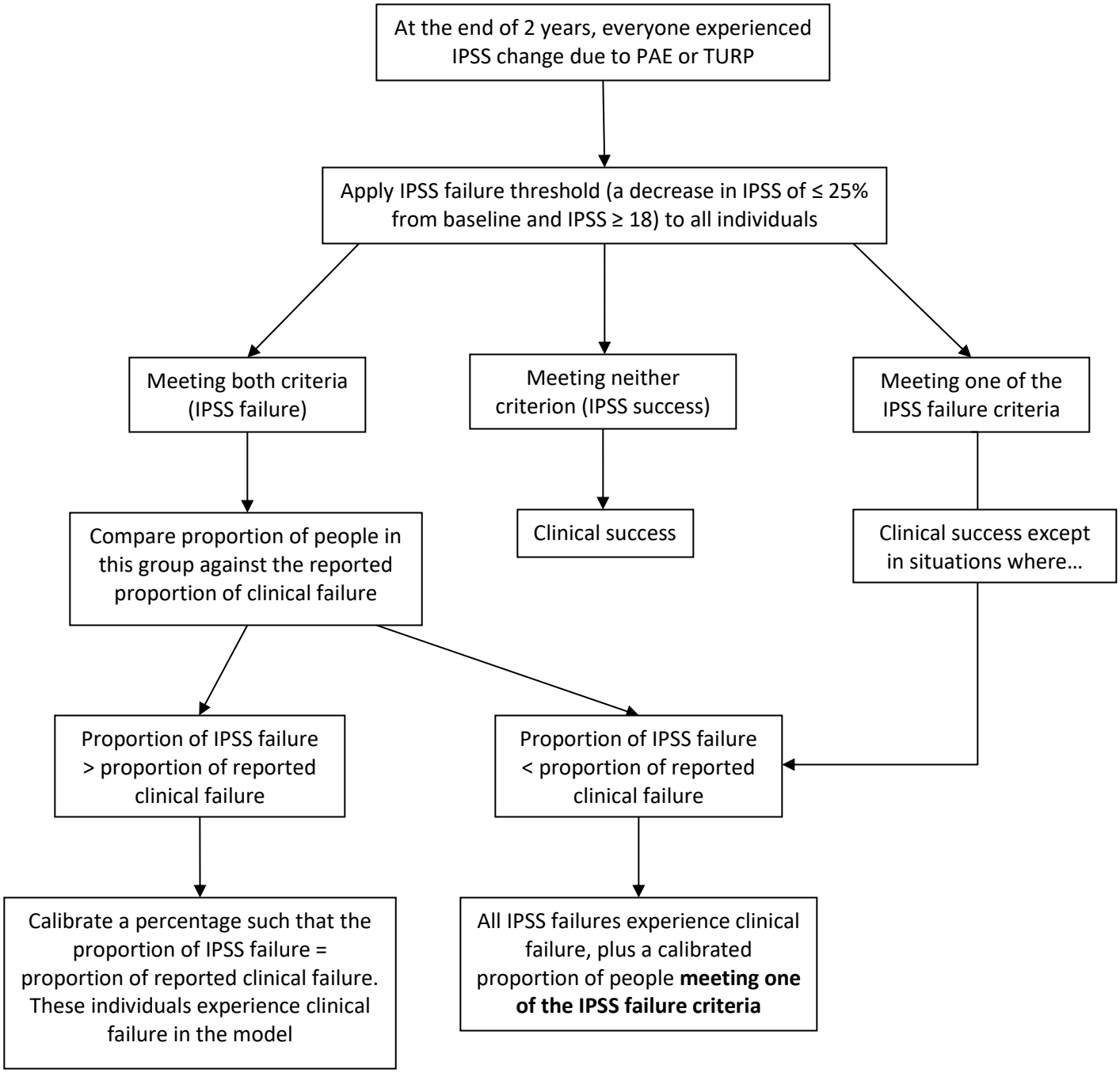

Figure 4 Schematic on Applying IPSS Failure Threshold to Model Clinical Failure at the End of 2 Years

Abbreviations: IPSS, International Prostate Symptom Score; PAE, prostatic artery embolization; TURP, transurethral resection of the prostate.

In other scenarios, due to varying follow-up periods in primary studies, we assumed people experienced clinical failure at the end of year 1 instead of year 2 (see Appendix 7, A and C for detailed scenario inputs).

Applying IPSS to Model Clinical Failure: Past 2 Years

Starting at year 3 and continuing to the end of time horizon, we applied a probability of potentially experiencing clinical failure at every cycle. Since the RCT by Gao et al[13] had only 2 years of follow-up, we estimated the long-term probability of clinical failure from the probability of reoperation as reported in observational studies.[68,74] We applied the IPSS failure threshold outlined in the long-term observational study by Pisco et al[68]: 1) a decrease in IPSS of ≤ 25% from baseline, and 2) IPSS ≥ 15. There was a slight variation in the IPSS failure thresholds used by Pisco et al,[68] where IPSS was ≥ 15, instead of ≥ 18 as outlined by Gao et al.[13] The first criteria of the IPSS failure threshold was consistent. We applied the same calibration process as described in Figure 4 to match our model parameters against the reported proportion of clinical failure.

The reported proportion of clinical failure that we obtained is presented in Table 21. Calibration is conducted in TreeAge Pro,[75] where the microsimulation model is programmed. Appendix 7B presents detailed notes on calibration and the calibrated parameters used in the model.

Table 21: Clinical Parameters (Technical and Clinical Failures) Used in the Economic Model—Reference Case

	Overall Probability	Lower 95% CI	Upper 95% CI	Potential Occurrence	Distribution	Source
PAE						
Technical failure	5.26%[a]	0%	11.06%	Perioperative	Beta	Gao et al, 2014[13]
Clinical failure				Ongoing	NA[b]	
End of year 2	9.26%[c]	—	—			Gao et al, 2014[13]
Year 3 to end of time horizon	3.86%[d]	—	—			Pisco et al, 2016[68]
TURP						
Clinical failure				Ongoing	NA[b]	
End of year 2	3.77%[c]	—	—			Gao et al, 2014[13]
Year 3 to end of time horizon	2.90%[d]	—	—			Strope et al, 2015[74]

Abbreviations: CI, confidence interval; IPSS, International Prostate Symptom Score; NA, not applicable; PAE, prostatic artery embolization; TURP, transurethral resection of the prostate.

[a]Probability applied as a one-time probability in the model.

[b]There are no 95% confidence intervals or distributions associated with these probabilities because we calibrated our model parameters against the mean probabilities only.

[c]IPSS criteria for clinical failure: decrease in IPSS of ≤ 25% and IPSS ≥ 18. Criteria is based on Gao et al, 2014.[13] In this model, those meeting both criteria would fail first, followed by those meeting one of the two components (if any).

[d]IPSS criteria for clinical failure: decrease in IPSS of ≤ 25% and IPSS ≥ 15. Criteria is based on Pisco et al, 2016.[68] In this model, those meeting both criteria would fail first, followed by those meeting one of the two components (if any).

OTHER ADVERSE EVENTS

In addition to technical and clinical failure, we also considered several other adverse events for TURP and PAE. The list of major adverse events were based on Gao et al,[13] the source of IPSS change in the reference case. Where appropriate (i.e., for a small number of major adverse events not reported by

Gao et al[13]), we obtained additional data from other RCTs included in the clinical evidence review as well as from the previous Ontario model involving TURP.[53,63,64,67]

For TURP, we included urinary retention, transurethral resection (TUR) syndrome, blood loss requiring transfusion, incontinence, urethral stricture or bladder neck contracture, ejaculatory dysfunction, and erectile dysfunction. Adverse events could occur within different time frames, such as perioperative, ongoing, or occurring within the first 1, 3, or 24 months. The varying time frames are based on the available study follow-up periods and data reported.[13,53,63,64,67] The probabilities reported in Table 22 are adjusted to 3-month probabilities in the model where appropriate.

For PAE, we included acute urinary retention as the only adverse event besides technical and clinical failures. This was the only adverse event reported in Gao et al.[13] In the model, acute urinary retention could only occur among those who experienced a technically successful procedure. Other adverse events were not considered after consulting other long-term observational studies and clinical experts as these adverse events were reported in a small proportion (1%) of people receiving PAE (i.e., non-target embolization and bladder wall ischemia),[68,76] and they resolved quickly without clinical consequence (e.g., post-embolization syndrome).[13] There are also concerns of long-term cancer risks related to potential radiation exposure.[77,78] However, there is a lack of consensus on the health effect due to the lack of long-term studies on the topic; as such, it was difficult to assign an appropriate monetary value (Derek Cool, MD, email communication, November 3, 2019).

Table 22: Clinical Parameters (Adverse Events) Used in the Economic Model—Reference Case

	Overall Probability	Lower 95% CI	Upper 95% CI	Potential Occurrence	Distribution	Source
PAE						
Acute urinary retention	25.93%[a]	14.24%	37.61%	First month	Beta	Gao et al, 2014[13]
TURP						
Perioperative death	0.10%[a]	0.08%	0.12%	Perioperative	Beta	Erman et al, 2018[67]
TUR syndrome	1.89%[a]	0%	5.50%	Perioperative	Beta	Gao et al, 2014[13]
Bleeding requiring transfusion	3.77%[a]	0%	8.90%	Perioperative	Beta	Gao et al, 2014[13]
Acute urinary retention	5.66%[a]	0%	11.88%	First month	Beta	Gao et al, 2014[13]
Incontinence	10.61%[a,b]	3.18%	18.03%	First 3 months	Beta	Carnevale et al, 2016,[39] Abt et al, 2018[53]
Urethral stricture or bladder neck contracture	4.17%[c]	0%	9.82%	First 2 years	Beta	Gao et al, 2014[13]
Erectile dysfunction	1.20%[d]	0.88%	1.51%	Ongoing	Beta	Erman et al, 2018[67]
Ejaculatory dysfunction				Ongoing	Beta	
Year 1 and Year 2	42.51%[d]	20.63%	54.40%			Erman et al, 2018[67]
Year 3 to end of time horizon	0.16%[d]	0.13%	0.20%			Erman et al, 2018[67]

Abbreviations: CI, confidence interval; PAE, prostatic artery embolization; TUR, transurethral resection; TURP, TUR of the prostate.

[a]Probability applied as a one-time probability in the model.

[b]Calculated as the weighted average of probabilities.

[c]Probability presented here is the probability over a 2-year period. Probability is adjusted in the model as 3-month probability to reflect the cycle length.

[d]Probability presented here is the probability over 1-year period (annual probability). Probability is adjusted in the model as 3-month probability to reflect the cycle length.

NATURAL PROGRESSION

An individual could start progressing (getting worse) based on natural history if the individual failed the maximum number of re-interventions after clinical failure (i.e., two TURPs, plus one PAE if the individual started in the PAE group). The natural IPSS progression is obtained from the literature (Table 23).[72]

For people experiencing clinical success, we assumed the IPSS would be stable for the time horizon of the model (6.5 years), based on the longest follow-up reported in observational studies on PAE as well as a previous Ontario economic evaluation on TURP.[67,68] Beyond 6.5 years (i.e., in a separate scenario with a longer time horizon of 10 years), IPSS would start progressing based on the natural history.[72] Note this assumption is only applicable to those experiencing clinical success. People experiencing clinical failure would go on to receive additional treatment (i.e., repeat TURP).

Table 23: Clinical Parameters (Natural IPSS Progression) Used in the Economic Model—Reference Case

	Mean	Lower 95% CI[a]	Upper 95% CI[a]	Distribution	Source
Natural progression (Annual)	0.18	−2.21	2.57	Normal	Jacobsen et al, 1996[72]

Abbreviations: CI, confidence interval; IPSS, International Prostate Symptom Score.

[a]95% confidence interval calculated using standard deviation to reflect individual-level variability.

MORTALITY

We obtained age- and gender-specific general mortality statistics from Statistics Canada Life Tables.[70] We also obtained from the literature the risk of perioperative death from TURP.[67]

HEALTH STATE UTILITIES

We obtained the utilities corresponding to the BPH severities (mild, moderate, and severe, based on IPSS) and disutilities of adverse events from the literature.[67,79,80] The utilities are listed in Table 24. Utilities associated with BPH severities are based on the Health Utilities Index Mark 2 (Health Utilities Inc., Dundas, ON, Canada).[67,79] The utilities applied in the first cycle corresponded to the severity level at baseline.

The disutilities of adverse events, derived using the standard gamble method, were taken from Ackerman et al.[80] The authors reported the utility of adverse events, a number between 0 (death) to 100 (perfect health), in two groups of individuals: the risk-averse (n = 6) and the non-risk-averse (n = 7) groups. We calculated the weighted average utility of the two groups for each adverse event. We then calculated the corresponding disutilities by dividing the utilities by 100 (to arrive at a number between 0 and 1) and then subtracted from 1. We also included the disutility associated with TURP for people undergoing and recovering from TURP (4 weeks of recovery) to reflect the effect of surgery on quality of life.[67,81] All adverse events are assumed to last for one cycle (3 months) based on the previous Ontario model involving TURP,[67] except for TUR syndrome, which has a duration of 1 week. Disutilities are adjusted based on their duration and are applied in each cycle where an individual experiences an adverse event.

Table 24: Utilities Used in the Economic Model

Health State	Mean	Lower 95% CI	Upper 95% CI	Distribution	Reference
BPH Health States				Beta	Baladi et al, 1996[79]
Mild	0.99	0.9	1		Erman et al, 2018[67]
Moderate	0.9	0.81	0.95		
Severe	0.79	0.73	0.85		
Surgical Intervention				Beta	
TURP	−0.05	−0.06	−0.04		Ackerman et al, 2000[80] Erman et al, 2018[67]
Adverse Events[a]				Beta	
TUR syndrome	−0.17	−0.23	−0.15		Erman et al, 2018[67]
Acute urinary retention	−0.18	−0.21	−0.15		Ackerman et al, 2000[80]
Ejaculatory dysfunction	−0.03	−0.04	−0.02		Ackerman et al, 2000[80]
Erectile dysfunction	−0.07	−0.08	−0.06		Ackerman et al, 2000[80]
Incontinence	−0.20	−0.23	−0.18		Ackerman et al, 2000[80]
Bladder neck contracture and urethral stricture	−0.06	−0.08	−0.04		Ackerman et al, 2000[80]

Abbreviations: BPH, benign prostatic hyperplasia; CI, confidence interval; TUR, transurethral resection; TURP, TUR of the prostate.

[a]The disutility of bleeding requiring transfusion is considered negligible.

Cost Parameters

We included the following types of resources and costs for PAE and TURP:

- Physician fees (procedural)
- Hospital costs (procedural)
- Follow-up costs
- Adverse events

All costs are reported in 2020 Canadian dollars except where otherwise noted. Where 2020 costs were not available, the Canadian health care component of the Statistics Canadian Consumer Price Index was used to adjust all costs to 2020 Canadian dollars.[82] Cost parameters used for the reference case are listed in Table 25. The detailed costing methods are described below.

PHYSICIAN FEES (PROCEDURAL)

Since there is not a PAE-specific billing code in the Schedule of Benefits,[83] a number of proxy codes were used to estimate physician fees in Ontario. Based on expert input, we assumed that, for PAE, physicians would bill for general catheterization (J021, J022, J014) and embolization procedures (J040, J047) (Kong Teng Tan, MD, email communication, November 22, 2019). The total cost of professional fees for PAE was estimated to be $682.81.

The OHIP billing code for TURP (S655) was obtained from the Ontario Schedule of Benefits.[83] The total cost of professional fees for TURP was estimated to be $615.71.

HOSPITAL COSTS (PROCEDURAL)

We obtained hospital costs for TURP and PAE from an Ontario costing study by Brown et al.[31] The study analyzed the hospital costs for TURP (n = 209) and PAE (n = 28) conducted from April, 2015, to March, 2017, at one institution in Ontario. For PAE, the costs included were related to the angiography suite, recovery care unit, and medication (e.g., painkillers). For TURP, the costs included pre-admission, operating room suite, anesthesia, post-anesthesia care unit, inpatient costs, and medication. The total hospital cost was $5,235 and $5,551 for PAE and TURP, respectively.

FOLLOW-UP COSTS

In the first year after the procedure, we assumed that the individuals who received PAE would have three follow-up consultations, and those who received TURP would have two follow-up visits with a urologist. Individuals from both groups have one annual visit with the urologist in subsequent years.

As a part of PAE and TURP follow-up in the first year, based on the literature and expert consultation, we also assumed the individual would undergo the following tests: urinalysis, serum creatinine, prostate-specific antigen (PSA) test, pressure flow study, and bladder/prostate ultrasound.[79] In subsequent years, both groups would have urinalysis, serum creatinine, and PSA testing done every year. Test costs were obtained from the Ontario Schedule of Benefits for Laboratory Services.[84]

ADVERSE EVENTS

We obtained one-time costs of the following adverse events from the literature: TUR syndrome, blood transfusion, ejaculatory dysfunction, erectile dysfunction, incontinence, acute urinary retention, urethral stricture/bladder neck contracture.[67,85] Costs were obtained from Canadian sources where possible.

Table 25: Costs Used in the Economic Model

Variable	Mean ($)	Lower 95% CI	Upper 95% CI	Distribution	Reference/Notes
Physician Fees					
PAE	682.81	512.11[a]	853.51[a]	Gamma	Schedule of Benefits:[83] J021, general catheterization; J022(×4) and J014(×2), selective catheterization; J040 and J047, embolization of multiple vessels
TURP	615.71	Fixed[a]	Fixed[a]	N/A	Schedule of Benefits:[83] S655, TURP plus anesthesiologist component (7 basic units and 4 time units)
Hospital Costs					
PAE	5,235.08	4,446.65	6,023.52	Gamma	Brown et al, 2019,[31] table 2[b] • Angiography suite and consumables: $4,495.56 • Recovery care unit: $703.88 • Pharmacy: $35.65
TURP	5,550.58	5,261.11	5,840.06	Gamma	Brown et al, 2019,[31] table 2[b] • Pre-admission: $276.56 • Operating room and consumables: $2,215.14 • Anesthesia: $336.06 • Recovery care unit: $709.86 • Inpatient costs: $1,854.25 • Pharmacy: $158.70
Follow-Up (Annual)					
PAE					
First year	282.03	202.03[c]	362.03[c]	Gamma	Schedule of Benefits,[83] Schedule of Benefits for Laboratory Services:[84] three physician visits (A355) and the following tests (once per year): urinalysis (G009), serum creatinine (L067), prostate-specific antigen test (L354), pressure flow study (G475), and bladder/prostate ultrasound (G900)
Subsequent years	85.58	5.58[c]	165.58[c]	Gamma	One physician visit (A355) and the following tests (once per year): urinalysis (G009), serum creatinine (L067), and prostate-specific antigen test (L354)

Variable	Mean ($)	Lower 95% CI	Upper 95% CI	Distribution	Reference/Notes
Follow-Up (Annual)					
TURP					
First year	202.03	122.03[c]	282.03[c]	Gamma	Two physician visits (A355) and the same tests as that of PAE in first year: urinalysis (G009), serum creatinine (L067), prostate-specific antigen test (L354), pressure flow study (G475) and bladder/prostate ultrasound (G900)
Subsequent years	85.58	5.58[c]	165.58[c]	Gamma	One physician visit (A355) and the same tests as that of PAE in subsequent years: urinalysis (G009), serum creatinine (L067) and prostate-specific antigen test (L354)
Adverse Events (Per Event)					
TUR syndrome	1,876.49	1,407.83	2,346.07	Gamma	Erman et al, 2018[67]
Blood transfusion	260.52	195.39	325.66	Gamma	Erman et al, 2018[67]
Ejaculatory dysfunction	328.98	308.41	411.22	Gamma	Erman et al, 2018[67]
Erectile dysfunction	415.58	328.98	519.47	Gamma	Erman et al, 2018[67]
Incontinence	328.98	308.41	411.22	Gamma	Erman et al, 2018[67]
Acute urinary retention	743.73	697.24	929.65	Gamma	Erman et al, 2018[67]
Urethral stricture or bladder neck contracture	1,714.73	1,607.56	2,143.42	Gamma	Erman et al, 2018[67]

Abbreviations: CI, confidence interval; PAE, prostatic artery embolization; TURP, transurethral resection of the prostate.

[a]Although fee codes are generally not expected to vary, because a number of proxy codes are used for PAE and codes used may vary in practice, we assumed ±25% around the mean cost as the 95% confidence interval for the physician fees of PAE. Because there is a specified fee code for TURP, we do not expect fees to vary. Therefore, we did not apply a 95% confidence interval for the physician fees of TURP.

[b]Original costs were reported in 2017 USD. We converted to 2017 CAD at $1.2986 CAD per USD, as reported by study authors. We then adjusted to 2020 CAD.

[c]We varied the number of follow-up visits to calculate the 95% confidence interval. PAE: two to four visits in the first year, and zero to two visits in subsequent years. TURP: one to three visits in the first year, and zero to two visits in subsequent years. The fee codes for lab tests and physician visit were not expected to vary.

Internal Validation

Formal internal validation was conducted by the secondary health economist. This included testing the mathematical logic of the model and checking for errors and accuracy of parameter inputs and equations.

Analysis

We conducted a reference case analysis and scenario analyses. Our reference case analysis adhered to CADTH guidelines[66] when appropriate and represents the analysis with the most likely set of input parameters and model assumptions.

We calculated the reference case by running probabilistic sensitivity analyses that simultaneously captured the uncertainty in all parameters that were expected to vary. The microsimulation model incorporates both patient variability and the underlying population uncertainty. Individual variability is captured using the mean and standard deviation, and the population uncertainty is captured using mean and standard error.[66] We used gamma distributions to represent cost parameters, beta distributions to represent probabilities and utilities, and normal distributions to represent age, starting IPSS, and changes in IPSS. The list of model variables and 95% confidence interval are given in Tables 20 to 25. The microsimulation model was run for 5,000 outer loops (parameter uncertainty) and 15,000 inner loops (individual variability), which were the number of loops required for the model outputs to stabilize. The microsimulation model was programmed using TreeAge Pro.[75]

We calculated mean costs and mean QALYs with credible intervals for each intervention assessed. We also calculated the mean incremental costs and incremental QALYs with credible intervals, and ICERs for PAE versus TURP. The results of the probabilistic sensitivity analysis are presented on a cost-effectiveness acceptability curve. We present uncertainty quantitatively as the probability that an intervention is cost-effective at specific willingness-to-pay values. We also present uncertainty qualitatively, in one of five categories defined by the Ontario Decision Framework[86]: highly likely, moderately likely, and uncertain to be cost-effective (80% to 100%, 60% to 79%, and 40% to 59% probability, respectively), or moderately or highly likely to not be cost-effective (20% to 39% and 0% to 19% probability, respectively).

SCENARIO ANALYSES

We conducted scenario analyses to address the structural uncertainty of the model:

- **Scenario 1:** Using an alternative primary study (Carnevale et al)[63] comparing PAE to TURP for the source of our IPSS inputs. Appendix 7A presents the detailed inputs for this scenario.
- **Scenario 2:** Comparing PAE to OSP instead of TURP. This is a scenario relevant to people who are ineligible for TURP (i.e., those with prostate glands too large to be eligible for TURP). Appendix 7C presents the detailed inputs for this scenario.
- **Scenario 3:** Assuming those who had initial PAE clinical success at 2 years but experienced clinical failure after 2 years would receive a second PAE instead of a TURP. We assumed the individual would receive TURP only if the second PAE also failed.
- **Scenario 4:** Assuming the treatment effect of PAE is shorter than TURP, lasting for 2 years post-procedure based on the follow-up period of the longest RCT available.[13] Two years after PAE, individuals who experienced clinical success would transition to the post-PAE

state. At this point, IPSS would progress based on the natural history rather than remaining stable (i.e., in the reference case). This scenario only affected the PAE group. In the TURP group, those who experienced clinical success would have stable improved IPSS until the end of the time horizon (6.5 years).

- **Scenario 5:** Using a 2-year time horizon. We conducted this scenario as there is limited RCT data on PAE beyond 2 years of follow-up.
- **Scenario 6:** Using a longer time horizon of 10 years to examine the long-term need for retreatment. We assumed that beyond 6.5 years after treatment (i.e., the time horizon of the reference case), IPSS progression would be based on natural history[67,72]

Results

Reference Case Analysis

Table 26 presents the results of our probabilistic reference case analysis for comparing PAE with TURP. Compared to TURP, PAE had an incremental cost of $328 (95% CrI: −$686 to $1,423) and a very small incremental QALY of 0.007 (95% CrI: −0.004 to 0.018). The ICER of PAE compared with TURP was $44,930 per QALY gained.

Table 26: Probabilistic Reference Case Analysis Results

Strategy	Average Total Costs (95% CrI)	Incremental Cost[a] (95% CrI)	Average Total QALYs (95% CrI)	Incremental QALY[b] (95% CrI)	ICER ($/QALY)
TURP	$7,771 ($7,279–$8,362)	—	5.415 (5.134–5.575)	—	—
PAE	$8,099 ($7,175–$9,089)	$328 (−$686 to $1,423)	5.422 (5.144–5.580)	0.007 (−0.004 to 0.018)	44,930

Abbreviations: CrI, credible interval; ICER, incremental cost-effectiveness ratio; PAE, prostatic artery embolization; QALY, quality-adjusted life year; TURP, transurethral resection of the prostate.

Note: all costs in 2020 CAD.

[a]Incremental cost = average cost (PAE) − average cost (TURP).

[b]Incremental effect = average effect (PAE) − average effect (TURP).

The cost breakdown of the two strategies (Table 27) revealed that the incremental cost ($328) was largely driven by the higher total procedural cost in the PAE group. It is important to note that this procedural cost included the cost of follow-up TURP for those failing PAE. Thus, even though the cost of PAE alone (i.e., hospital cost, $5,240) was lower than TURP (i.e., hospital cost, $5,903), the total procedural cost in the PAE strategy exceeded that of the TURP strategy. In contrast, the cost of adverse events for TURP was almost twice the cost for PAE.

Table 27: Cost Breakdown of Reference Case Analysis Results

	PAE ($)	TURP ($)
Procedural		
Physician	802 (attributable to follow-up TURP: $117)	655
Hospital	6,294 (attributable to follow-up TURP: $1,055)	5,903
Follow-up	706 (attributable to follow-up TURP: $89)	621
Adverse Events	296 (attributable to follow-up TURP: $102)	591
Total[a]	**8,099**	**7,771**

Abbreviations: PAE, prostatic artery embolization; TURP, transurethral resection of the prostate.
Note: all costs in 2020 CAD.
[a]Numbers may appear inexact due to rounding.

Figure 5 presents the cost-effectiveness acceptability curve, which shows the probability of PAE being cost-effective compared to TURP across a range of willingness-to-pay thresholds. At commonly used willingness-to-pay values of $50,000 and $100,000 per QALY, PAE is 52% and 68% likely to be cost-effective, respectively. The scatter plot of 1,000 simulated pairs of incremental costs and effects in the cost-effectiveness plane is provided in Figure A1 (Appendix 7D).

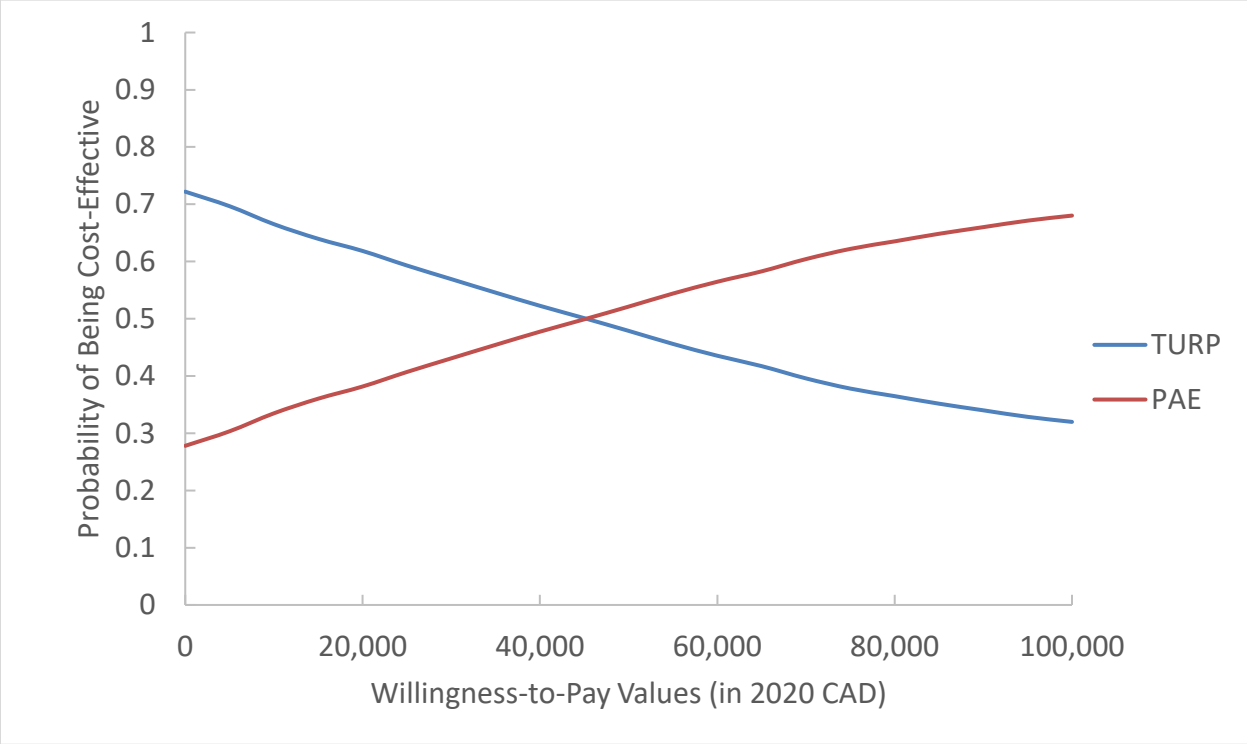

Figure 5: Cost-Effectiveness Acceptability Curve—PAE Versus TURP, Reference Case

Scenario Analyses

Table 28 presents the results from our scenario analyses. In scenario 1, the cost-effectiveness of PAE varied when another RCT by Carnevale et al[63] was used as the source of clinical inputs (e.g., IPSS change). The results showed that PAE was more costly and less effective compared to TURP (i.e., PAE is dominated by TURP). In scenario 2, when we compared PAE to OSP, PAE was less costly (−$1,229) and generated fewer QALYs (−0.12) than OSP. Compared with OSP, PAE had an ICER of $10,249 saved per QALY lost. At a willingness-to-pay of $50,000 per QALY, PAE is very unlikely to be cost-effective compared to OSP (2% probability).

Similar to our reference case analysis, in scenarios 3 to 6, where we used the Gao et al study[13] as our source of IPSS reduction, the incremental QALYs were very small (range: −0.01 to 0.03). Since incremental QALY is the denominator used in calculating ICER, near-zero incremental QALYs in these scenarios resulted in different ICERs across scenarios even though the numerical difference across incremental QALYs was small. In scenario 3, where we assumed PAE was repeated if people in the PAE strategy experienced clinical failure after 2 years, the incremental costs were similar to the reference case. However, a small decrease in incremental QALYs (from 0.007 in the reference case to 0.003 in the scenario) led to a much larger ICER in the scenario ($103,067 per QALY gained). In scenario 4 where PAE had a shorter treatment effect, PAE had slightly lower QALYs than TURP. Since the cost of PAE was also higher than TURP, PAE was dominated (more costly and less effective) by TURP. In scenario 5, where we used a 2-year time horizon, PAE was slightly less costly (incremental cost $143) and less effective than TURP (incremental QALY 0.01). PAE had lower cost likely because the shorter time horizon could not capture the long-term clinical failure (especially in PAE) after 2 years. In this scenario, PAE has an ICER of $10,310 saved per QALY lost. Finally, in scenario 6, where we used a 10-year time horizon, PAE remained more costly and slightly more effective than TURP (ICER of PAE compared to TURP: $10,006 per QALY gained).

Table 28: Scenario Analysis Results

Strategy	Average Total Costs (95% CrI)	Incremental Cost[a] (95% CrI)	Average Total QALYs (95% CrI)	Incremental QALY[b] (95% CrI)	ICER ($/QALY)
Scenario 1: Alternative Primary Study (PAE vs. TURP): Carnevale et al, 2016[39]					
TURP	$7,577 ($7,089–$8,169)	—	5.48 (5.22–5.63)	—	
PAE	$9,076 ($7,933–$10,423)	$1,499 ($278–$2,877)	5.34 (5.07–5.53)	−0.14 (−0.22 to −0.05)	PAE dominated (more costly, less effective)
Scenario 2: PAE vs. OSP					
OSP	$9,681 ($8,768–$10,640)	—	5.51 (5.23–5.65)	—	
PAE	$8,449 ($7,491–$9,504)	−$1,231 (−$2,457 to $69)	5.39 (5.12–5.56)	−0.12 (−0.18 to −0.04)	PAE vs. OSP: $10,241 saved per QALY lost
Scenario 3: Repeat PAE					
TURP	$7,771 ($7,279–$8,362)	—	5.41 (5.13–5.57)	—	

Strategy	Average Total Costs (95% CrI)	Incremental Cost[a] (95% CrI)	Average Total QALYs (95% CrI)	Incremental QALY[b] (95% CrI)	ICER ($/QALY)
PAE	$8,122 ($7,171–$9,138)	$351 (−$696 to $1,477)	5.42 (5.14–5.58)	0.003 (−0.01 to 0.02)	PAE vs. TURP: $103,067 per QALY gained
Scenario 4: Shorter Treatment Effect for PAE					
TURP	$7,771 ($7,279–$8,362)	—	5.64 (5.31–5.83)	—	
PAE	$8,080 ($7,158–$9,069)	$310 (−$706 to $1,406)	5.63 (5.30–5.83)	−0.006 (−0.02 to 0.01)	PAE dominated (more costly, less effective)
Scenario 5: 2-Yr Time Horizon					
TURP	$6,983 ($6,618–$7,382)	—	1.77 (1.68–1.83)	—	
PAE	$6,839 ($5,965–$7,766)	−$143 (−$1,058 to $848)	1.75 (1.67–1.81)	−0.01 (−0.03 to 0.001)	PAE vs. TURP: $10,310 saved per QALY lost
Scenario 6: 10-Yr Time Horizon					
TURP	$8,270 ($7,668–$9,045)	—	7.77 (7.37–8.00)	—	
PAE	$8,615 ($7,641–$9,689)	$345 (−$794 to $1,565)	7.81 (7.41–8.03)	0.03 (0.02–0.05)	PAE vs. TURP: 10,006 per QALY gained

Abbreviations: CrI, credible interval; ICER, incremental cost-effectiveness ratio; OSP, open simple prostatectomy; PAE, prostatic artery embolization; QALY, quality-adjusted life year; TURP, transurethral resection of the prostate.

[a]Incremental cost = strategy with the higher average cost – strategy with the lower average cost.

[b]Incremental effectiveness = strategy with the higher average QALYs – strategy with the lower average QALYs.

Discussion

Although the existing costing studies from the economic evidence review suggest that PAE may be less costly than TURP, our reference case analysis showed comparable QALYs and slightly higher cost for PAE compared to TURP. In our reference case, it is uncertain whether PAE is cost-effective (i.e., 52% likely to be cost-effective) compared with TURP (ICER: $44,930 per QALY) at a willingness-to-pay of $50,000 per QALY gained. A key difference in PAE costs reported in earlier studies and our analysis is the consideration of clinical failure and reintervention after PAE. Our analysis showed that the procedural cost of PAE alone may be lower than TURP; however, when considering the rate of technical failure and the higher rate of clinical failure for PAE compared to TURP, the total cost, including downstream treatment due to PAE failure, slightly exceeded that of TURP.

The scenario analyses showed that the cost-effectiveness of PAE compared with TURP is uncertain and there is little evidence of PAE being cost-effective overall. When we used alternative IPSS data that was more favourable towards TURP (e.g., Carnevale et al[63]), PAE was dominated (more costly and less effective) by TURP. The cost-effectiveness of PAE also varied depending on the comparator (i.e., TURP or OSP). In the scenario comparing PAE to OSP, PAE was found to be less costly than OSP, which was consistent with the costing analysis reported in the literature.[87] PAE also led to fewer QALYs than OSP, giving PAE an ICER of $10,249 saved per QALY lost. However, there is only one directly applicable study

comparing PAE and OSP, and an RCT on this comparison has not been conducted. Higher quality studies may be needed to further examine the cost-effectiveness of PAE compared to OSP.

We modelled IPSS change and used this to classify the severity of BPH and to estimate QALYs. We were able to model the gradual IPSS change over the 2-year period to reflect the IPSS data reported in the RCT by Gao et al.[13] We did not model using other RCTs on PAE versus TURP as alternative sources of IPSS, such as the recently published RCT conducted by Insausti et al.[16] Clinical failure rates were not reported in the Insausti study, thus we were unable use this study to examine the potential costs and QALYs associated with any re-interventions. Similarly, we were unable to use the RCT conducted by Abt et al[53] as the study had 3 months of follow-up only, and it was not feasible to model the long-term trajectory of the condition following the interventions.

Although clinical failure was reported separately to IPSS in the primary study, we wanted to capture it and its relation to IPSS in our model. We did this by calibrating the proportion of people meeting the IPSS threshold criteria for clinical failure to match the literature. We acknowledge that factors other than IPSS (e.g., other symptom indicators such as peak urinary flow and quality of life questionnaire score) are involved in assessing intervention failure in the clinical setting. However, IPSS is likely correlated with these symptom indicators, thus can still act as a proxy for assessing clinical failure.

We also made assumptions around the treatment effect for those experiencing clinical success: we assumed all clinically successful treatments led to stable IPSS for 6.5 years. However, there is some uncertainty around how long the treatment effect of PAE will last due to a limited number of long-term studies. It is possible that more established surgical treatments (e.g., TURP, OSP) may have longer lasting treatment effects than PAE, beyond 6.5 years (Dean Elterman, MD, email communication, January 20, 2020). Assuming all treatments have the same longevity could have produced results that were more favourable towards PAE. In scenario 4 we made a more conservative assumption and assumed that the treatment effect of PAE was shorter than TURP. Prostatic artery embolization was found to be more costly and less effective than TURP (dominated). This scenario confirmed that the cost-effectiveness of PAE is influenced by the longevity of the PAE treatment effect relative to that of TURP.

Although PAE was more costly than TURP overall, the cost of adverse events for TURP ($296) was higher than that of PAE ($102), as TURP is more invasive and has more adverse events associated with the surgery. TURP may take longer to recover, which could bring about additional costs from the patient and societal perspectives (e.g., lost productivity, cost of care giver, etc.). However, more research may be needed to examine the long-term effects of PAE on potential adverse events such as ejaculatory dysfunction, effect of contrast dye, and risk of malignancy from radiation exposure. Ejaculatory dysfunction is reported in 14 of 48 PAE patients (29%) in one 3-month RCT by Abt et al,[53] although longer RCTs have yet to produce comparable results (ejaculatory dysfunction was reported in only one or two individuals in other RCT cohorts).[16,63] There is also controversy over the effect of contrast dye and radiation exposure from PAE, and it would be difficult to assign an appropriate monetary value given the current lack of long-term evidence on these adverse events (Derek Cool, MD, email communication, November 3, 2019).

In costing the resources for PAE, we did not consider the potential cost of building additional angiography suites. We did not expect PAE alone to be the major driver in building new angiography units in Ontario given the anticipated slow PAE uptake (Dean Elterman, MD, email communication, November 27, 2019). However, we acknowledge that including additional costs for angiography suites would likely have significant cost implications to the health care system. If such costs are included in this

analysis, we would anticipate PAE to have a higher total cost (and, therefore, higher incremental cost), leading to a higher ICER.

Strengths and Limitations

Our analysis had several strengths. We used a microsimulation model, which allowed us to incorporate individual variability in baseline IPSS and IPSS change. We modelled gradual IPSS change based on the original primary study. We also considered stepped care for people with moderate to severe BPH, which was more reflective of real clinical practices. Our economic evaluation provided additional insights to the existing costing analyses, which were limited on the long-term costs of post-operative adverse events and re-intervention. In addition, we calibrated the proportion of people meeting the IPSS failure thresholds to match the reported proportion of clinical failure. However, given the chronic nature of BPH, this model has a relatively short time horizon due to the lack of longer-term studies. Our time horizon may not be enough to fully examine re-intervention of treatments and long-term post-intervention progression of BPH.

Conclusions

Our primary economic evaluation found that, compared with TURP, PAE is more costly and has a small QALY increase due to fewer adverse events. The ICER of PAE versus TURP is $44,930 per QALY gained. At a willingness-to-pay of $50,000 per QALY, the cost-effectiveness of PAE is uncertain. Compared with OSP, PAE is less costly and less effective. The ICER of PAE versus OSP is $10,241 saved per QALY lost and at a willingness-to-pay of $50,000 per QALY, PAE is unlikely to be cost-effective.

Budget Impact Analysis

Research Question

From the perspective of the Ontario Ministry of Health, what is the potential budget impact of publicly funding prostatic artery embolization (PAE) for people with benign prostatic hyperplasia (BPH)?

Methods

Analytic Framework

We estimated the budget impact of publicly funding PAE for people with BPH using the cost difference between two scenarios: (1) current clinical practice with limited public funding for PAE (the current scenario) and (2) anticipated practice with public funding for PAE (the new scenario). Figure 6 presents the budget impact model schematic.

We conducted a reference case analysis and sensitivity analyses. Our reference case analysis represents the analysis with the most likely set of input parameters and model assumptions. Our sensitivity analyses explored how the results are affected by varying input parameters and model assumptions.

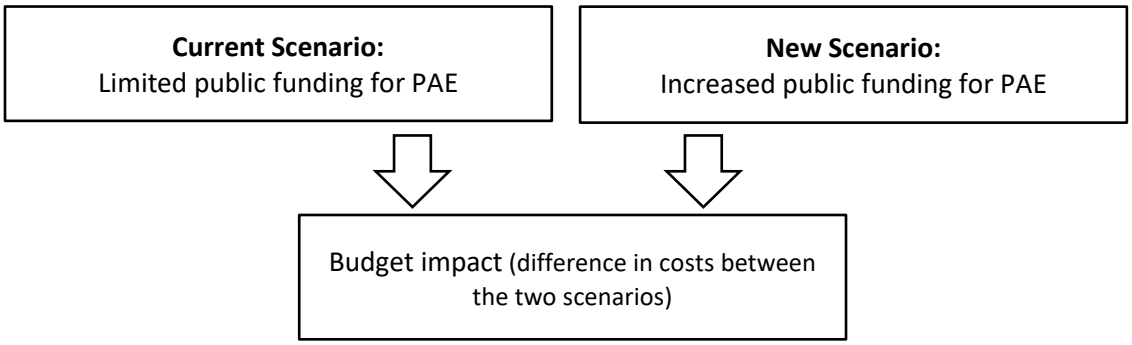

Figure 6: Schematic Model of Budget Impact

Abbreviation: PAE, prostatic artery embolization.

Key Assumptions

The assumptions of the primary economic evaluation are relevant to our budget impact analysis. Based on expert input, we made several additional assumptions that are specific to our budget impact analysis:

- There are currently about 40 PAE procedures conducted per year in Ontario. The procedures are all conducted at one centre (Kong Teng Tan, MD, phone communication, September 20, 2019). The costs of these procedures are included in the current scenario as they are presently funded through the global hospital budget and OHIP physician fees (using proxy codes). We assumed this volume would remain constant from year to year in the current scenario
- In the new scenario (i.e., public funding for PAE), there would be a slow uptake of PAE in the next 5 years because there are a limited number of centres in Ontario that are equipped with the appropriate angiography facilities and specialized interventional radiology expertise

Target Population

While most cases of BPH are managed conservatively (e.g., through watchful waiting),[57] we are specifically interested in people presenting with moderate to severe symptoms who may consider PAE or other surgical alternatives. We assume this group has refused or failed medication or other earlier lines of treatment (e.g., lifestyle interventions), as the most common reason for considering surgical or minimally invasive interventions is the failure to respond to BPH medications.[88] People with bothersome symptoms that do not respond to medication are typically recommended TURP. If PAE is implemented, it may be a less invasive alternative.[57] In addition, PAE may be a favourable alternative for those with very large prostate glands, who may otherwise undergo OSP (Dean Elterman, MD, email communication, November 27, 2019). Based on the expert opinion that PAE will act as an alternative to TURP or OSP, we included in our target population people with BPH who undergo either PAE, TURP, or OSP. We assumed people who respond to medications or other earlier lines of treatment (e.g., lifestyle changes) would not receive PAE.

We estimated the number of people receiving TURP and OSP using data from IntelliHealth Ontario, a health administrative database.[89] We obtained the number of people receiving TURP and OSP using fee codes from the Ontario Schedule of Benefits: S655 (TURP), S650 (OSP, retropubic simple prostatectomy), S645 (OSP, perineal prostatectomy), and S647 (OSP, suprapubic prostatectomy). From the most recent 5-year data (2013–2017) and the International Statistical Classification of Diseases and Related Health Problems (ICD) code for BPH (600.01),[90] we found that about 5,400–5,700 people diagnosed with BPH each year underwent TURP, and about 40–80 people underwent OSP. We then estimated the numbers of people who will receive TURP or OSP in the next 5 years. We broke the volume of people down by 5-year age groups in IntelliHealth Ontario, excluding a small number of individuals with missing age group information, and estimated future volumes within the respective age groups based on the male population projections from the Ontario Ministry of Finance.[91] Using the volumes of TURP and OSP in 2017, we applied the projected annual population growth from 2018 to 2025 within the respective age groups. The projected volumes of TURP and OSP in the next 5 years ranged from 6,329 to 7,234 and from 78 to 90, respectively.

For the PAE population, based on expert consultation, we assumed currently around 40 PAE procedures are conducted per year in Ontario at one centre. The volume of PAE has been constant from year to year (Kong Teng Tan, MD, phone communication, September 20, 2019). These PAE procedures are presently funded by the Ministry of Health through the global hospital budget and OHIP physician fees (proxy codes). We included 40 annual PAE procedures in our current scenario to capture the current cost incurred by the Ministry of Health. We assumed that the volume of PAE remains constant each year in the current scenario.

The sum of the three groups (PAE, TURP, and OSP) is around 6,400 to 7,300 people each year (Table 29).

Table 29: Target Population

	Year 1	Year 2	Year 3	Year 4	Year 5
Target Population/Volume (N)	6,447	6,668	6,896	7,129	7,364
PAE	40	40	40	40	40
TURP	6,329	6,547	6,772	7,002	7,234
OSP	78	81	84	87	90

Abbreviations: OSP, open simple prostatectomy; PAE, prostatic artery embolization; TURP, transurethral resection of the prostate.

Source: TURP and OSP volumes were based on 2017 data provided by IntelliHealth Ontario and projected based on the male population projections for 2018 to 2025 provided by the Ontario Ministry of Finance.[91]

Uptake of the New Intervention and New Intervention Mix

It is difficult to estimate the uptake of PAE if it is publicly funded. While we expect there to be continued use of PAE in the centre that is currently providing it, we anticipate there may be a slow uptake in other centres. We expect this because PAE requires specialized angiography units and additional interventional radiology training. Some Canadian sites have decided not to (or that they cannot) implement the procedure because they lack sufficient time and resources.[57] We assumed no new angiography units would be built and only a limited number of centres in Ontario would be equipped with the appropriate facilities and expertise. We assumed there would be slow uptake, with 10 additional PAE procedures being performed each year, increasing from 50 procedures in year 1 to 90 procedures in year 5.

In the reference case analysis, we assumed PAE would replace only TURP (Table 30). In scenario analyses, we assumed that PAE would replace only OSP, or a mix of both.

Table 30: Uptake of PAE—Reference Case

	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Target Population (n)	6,447	6,668	6,896	7,129	7,364	34,505
Current Scenario: Funding Via Hospital Global Budget						
PAE	40	40	40	40	40	200
TURP	6,329	6,547	6,772	7,002	7,234	33,884
OSP	78	81	84	87	90	420
New Scenario: Public Funding for PAE						
PAE	50	60	70	80	90	350
TURP	6,319	6,527	6,742	6,962	7,184	33,734
OSP	78	81	84	87	90	420

Abbreviations: OSP, open simple prostatectomy; PAE, prostatic artery embolization; TURP, transurethral resection of the prostate.

Resources and Costs

The undiscounted, annual per person costs for PAE, TURP, and OSP were derived from our primary economic evaluation (see Table 31). Costs were broken into procedural costs (physician fees and hospital costs), follow-up, and adverse event-related costs. The annual per person costs were used in calculating the total costs of both the current and new scenarios.

The cost per person in year 1 from the PAE group ($6,748) was slightly higher than that of TURP ($6,699), but lower than the OSP group ($8,914). Similar trends were observed for the procedural costs. The adverse events for TURP procedure was the highest of the three interventions.

The first-year procedural cost for the PAE group included the cost of TURP ($337) in people who experienced PAE technical failure (i.e., failure to achieve embolization), who we assumed would have received a follow-up TURP in the first year. As such, the per-person procedural cost of the PAE procedure alone ($5,925) is lower than TURP ($6,164) and OSP ($8,642). However, the cost of additional treatment due to PAE technical failure added to the overall procedural cost.

There were also procedural costs incurred at year 3 for PAE and TURP, as clinical failure was assessed at the end of year 2, and people who experienced clinical failure received a secondary treatment at year 3. There was also a smaller proportion of people who received secondary treatment in years 4 and 5. The procedural costs were slightly higher for the PAE group in year 5 than in year 4. This is due to a small percentage of people who failed their secondary treatment (received at year 3), who received another treatment at year 5. The slight increase in procedural costs in year 5 compared to year 4 is also observed in TURP, although the difference is much smaller and appeared negligible due to rounding.

There were procedural costs in year 2 for OSP because clinical failure in this group was assessed at the end of year 1 instead of year 2 due to varied follow-up and reporting in primary studies.[13,65] Thus, those who had OSP and experienced clinical failure at the end of year 1 received an additional treatment in year 2.

Table 31: Annual Per-Person Cost—Reference Case

	Year 1	Year 2	Year 3	Year 4	Year 5
PAE					
Procedural	$6,261	$0	$705	$33	$75
Physician	$719	$0	$70	$3	$7
Hospital	$5,543	$0	$635	$30	$67
Follow-up	$277	$85	$94	$81	$79
Adverse events	$209	$11	$40	$25	$7
Total	**$6,748**	**$97**	**$839**	**$140**	**$160**
TURP					
Procedural	$6,164	$0	$358	$14	$14
Physician	$616	$0	$36	$1	$1
Hospital	$5,548	$0	$322	$13	$13
Follow-up	$200	$84	$88	$81	$78
Adverse events	$335	$208	$23	$17	$7
Total	**$6,699**	**$292**	**$469**	**$112**	**$100**
OSP					
Procedural	$8,642	$304	$3	$0	$0
Physician	$868	$31	$0	$0	$0
Hospital	$7,775	$274	$3	$0	$0
Follow-up	$200	$88	$83	$452	$79
Adverse events	$72	$43	$2	$0	$0
Total	**$8,914**	**$435**	**$88**	**$81**	**$79**

Abbreviations: OSP, open simple prostatectomy; PAE, prostatic artery embolization; TURP, transurethral resection of the prostate.

Internal Validation

The secondary health economist conducted formal internal validation. This process included checking for errors and ensuring the accuracy of parameter inputs and equations in the budget impact analysis.

Analysis

For the reference case analysis, we calculated the budget required to publicly fund PAE for people with BPH in Ontario. This was calculated as the cost difference between the new scenario (publicly funding for PAE) and the current scenario (limited public funding for PAE). We presented total costs along with cost breakdowns by intervention (i.e., PAE, TURP, and OSP).

We also conducted the following scenario analyses by altering the proportions of TURP and OSP procedures switched by PAE:

- Scenario 1: 0% TURP, 100% OSP

- Scenario 2: 25% TURP, 75% OSP
- Scenario 3: 50% TURP, 50% OSP
- Scenario 4: 75% TURP, 25% OSP

Results

Reference Case

Table 32 presents the results of our reference case budget impact analysis. In the current scenario, in which limited funding for PAE is provided through hospital global budgets, the total cost per year is between $43.37 million and $56.23 million and mainly consists of the cost of TURP ($42.40 million to $55.05 million per year). In the new scenario, in which PAE is publicly funded, the total cost per year is $43.37 million to $56.24 million. The cost of PAE increased from $0.27 million to $0.32 million per year in the current scenario to $0.34 million to $0.69 million per year in the new scenario. This increase in the cost of PAE was offset by the decrease in costs of TURP, with about $1.067 million over the 5-year period. We estimate that over 5 years, providing public funding to PAE would lead to an additional cost of $11,400 over 5 years, as compared with funding PAE with limited uptake through hospital global budgets (i.e., the current scenario).

Table 32: Budget Impact Analysis Results—Reference Case

	Budget Impact (in $ Millions CAD)[a,b]					
Scenario	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Total**
Current Scenario, PAE Funding Via Hospital Global Budget						
PAE	0.27	0.27	0.31	0.31	0.32	1.48
TURP	42.40	45.70	50.25	52.66	55.05	246.06
OSP	0.70	0.76	0.79	0.83	0.86	3.94
Total	**43.37**	**46.73**	**51.35**	**53.80**	**56.23**	**251.48**
New Scenario, Public Funding of PAE						
PAE	0.34	0.41	0.52	0.60	0.69	2.56
TURP	42.33	45.57	50.03	52.38	54.69	244.99
OSP	0.70	0.76	0.79	0.83	0.86	3.94
Total	**43.37**	**46.73**	**51.35**	**53.81**	**56.24**	**251.49**
Budget Impact						
PAE	0.067	0.136	0.213	0.291	0.371	1.078
TURP	−0.067	−0.137	−0.211	−0.287	−0.364	−1.067
OSP	—	—	—	—	—	—
Total	**0.0005**	**-0.0010**	**0.0013**	**0.0038**	**0.0069**	**0.0114**

Abbreviations: OSP, open simple prostatectomy; PAE, prostatic artery embolization; TURP, transurethral resection of the prostate.

[a]Negative costs indicate savings.

[b]Numbers may appear inexact due to rounding.

Scenario Analysis

Table 33 presents the results of our scenario analyses when we assumed that PAE would replace some OSP procedures. All scenarios resulted in cost savings, with the 5-year total budget impact ranging from a cost savings of $0.07 million (Scenario 3) to $0.31 million (Scenario 4). The savings were due to the higher per-person cost of OSP relative to PAE.

Table 33: Budget Impact Analysis Results—Scenario Analyses

Scenario	Budget Impact (in $ Millions CAD)[a,b]					
	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Scenario 1: Proportion of PAE Cases: 0% TURP, 100% OSP						
PAE	0.07	0.14	0.21	0.29	0.37	1.08
TURP	—	—	—	—	—	—
OSP	−0.09	−0.18	−0.28	−0.37	−0.47	−1.39
Total	**−0.02**	**−0.05**	**−0.06**	**−0.08**	**−0.10**	**−0.31**
Scenario 2: Proportion of PAE Cases: 25% TURP, 75% OSP						
PAE	0.07	0.14	0.21	0.29	0.37	1.08
TURP	−0.02	−0.03	−0.05	−0.07	−0.09	−0.27
OSP	−0.07	−0.14	−0.21	−0.28	−0.35	−1.04
Total	**−0.02**	**−0.04**	**−0.05**	**−0.06**	**−0.07**	**−0.23**
Scenario 3: Proportion of PAE Cases: 50% TURP, 50% OSP						
PAE	0.07	0.14	0.21	0.29	0.37	1.08
TURP	−0.03	−0.07	−0.11	−0.14	−0.18	−0.53
OSP	−0.04	−0.09	−0.14	−0.19	−0.23	−0.69
Total	**−0.01**	**−0.02**	**−0.03**	**−0.04**	**−0.05**	**−0.15**
Scenario 4: Proportion of PAE Cases: 75% TURP, 25% OSP						
PAE	0.07	0.14	0.21	0.29	0.37	1.08
TURP	−0.05	−0.10	−0.16	−0.22	−0.27	−0.80
OSP	−0.02	−0.05	−0.07	−0.09	−0.12	−0.35
Total	**−0.01**	**−0.01**	**−0.02**	**−0.02**	**−0.02**	**−0.07**

Abbreviations: OSP, open simple prostatectomy; PAE, prostatic artery embolization; TURP, transurethral resection of the prostate.

[a]Negative costs indicate savings.

[b]Numbers may appear inexact due to rounding.

Discussion

The budget impact analysis showed that publicly funding PAE for those with BPH would lead to an additional cost of $11,400 over 5 years. When we assumed PAE would replace some OSP procedures, it resulted in some cost savings because the per-person cost of PAE is lower than that of OSP (scenarios 1–4).

In the reference case analysis, we assumed a low uptake of PAE procedures. A higher uptake may necessitate building additional angiography suites. The capital cost may be significant and there may be other additional costs (positive budget impact). Currently in Ontario, roughly 20 to 30 major teaching hospitals and larger community hospitals have the facilities to perform PAE (Kong Teng Tan, MD, email communication, November 22, 2019). Building and equipping a new angiography suite in general costs approximately $2 million to $4 million.[92] However, we did not expect PAE to be a major driver in building new angiography suites in Ontario given the additional intervention radiology required and anticipated

slow PAE uptake (Dean Elterman, MD, email communication, November 27, 2019). Furthermore, PAE may be more clinically suitable for some people, such as those who refuse to undergo or are ineligible for standard procedures such as TURP (Dean Elterman, MD, email communication, November 27, 2019).

While providing public funding to PAE may not lead to a large budgetary increase, the primary economic evaluation showed that the cost-effectiveness of PAE compared with TURP is uncertain, and PAE is unlikely to be cost-effective compared with OSP.

Strengths and Limitations

Our analysis had several strengths. We were able to obtain the volume of people receiving TURP and OSP from Ontario administrative databases, and we forecasted future volumes according to Ontario population projections. We also examined the proportion of PAE procedures that would replace other interventions. However, our analysis also had limitations. A 5-year budget impact may not be sufficiently long to account for re-interventions that may occur beyond 5 years. Our analysis also assumed a slow uptake and did not consider the cost of building additional angiography suites. PAE uptake that is higher than expected may warrant additional capital costs.

Conclusions

Publicly funding PAE in people with BPH would lead to an additional cost of $11,400 over the next 5 years.

Preferences and Values Evidence

Objective

The objective of this analysis was to explore the underlying values, needs, and priorities of those who have lived experience with benign prostatic hyperplasia (BPH) and potential treatment options, such as prostatic artery embolization (PAE).

Background

Exploring patient preferences and values provides a unique source of information about people's experiences of a health condition and the health technologies or interventions used to manage or treat that health condition. It includes the impact of the condition and its treatment on the person with the health condition, their family and other caregivers, and the person's personal environment. Engagement also provides insights into how a health condition is managed by the province's health system.

Information shared from lived experience can also identify gaps or limitations in published research (e.g., outcomes important to those with lived experience that are not reflected in the literature).[93-95] Additionally, lived experience can provide information and perspectives on the ethical and social values implications of health technologies or interventions.

Because the needs, preferences, priorities, and values of those with lived experience in Ontario are important to consider to understand the impact of the technology in people's lives, we may speak directly with people who live with a given health condition, including those with experience of the technology or intervention we are exploring.

For this analysis, we examined the preferences and values of people who have lived experience with BPH and who may consider seeking out a treatment option such as prostatic artery embolization. We examined these preferences and values through direct engagement with people with applicable lived-experience through phone interviews.

Direct Patient Engagement

Methods

PARTNERSHIP PLAN

The partnership plan for this health technology assessment focused on consultation to examine the experiences of people with lived experience with BPH and who may have received prostatic artery embolization. We engaged people via phone interviews.

We used a qualitative interview, as this method of engagement allowed us to explore the meaning of central themes in the experiences of people with lived experience with BPH.[96] The sensitive nature of exploring people's experiences of a health condition and their quality of life are other factors that support our choice of an interview methodology.

PARTICIPANT OUTREACH

We used an approach called purposive sampling,[97-100] which involves actively reaching out to people with direct experience of the health condition and health technology or intervention being reviewed.

We approached a variety of partner organizations and clinical experts to spread the word about this engagement activity and to contact people with experience with BPH and, potentially, PAE.

Inclusion Criteria

We sought to speak with people with lived experience of BPH and PAE, or who may seek out PAE in the future. Participants did not need to have direct experience with this procedure to participate.

Exclusion Criteria

We did not set exclusion criteria for people who otherwise met our inclusion criteria.

Participants

For this project, we spoke with four people with lived experience with BPH. Three of the participants had received prostatic artery embolization, while the final individual was exploring options to have it done in the future. Participants were located in southern Ontario or the Ottawa area.

APPROACH

At the beginning of the interview, we explained the role of our organization, the purpose of this health technology assessment, the risks of participation, and how participants' personal health information would be protected. We gave this information to participants both verbally and in a letter of information (Appendix 8), if requested. We then obtained participants' verbal consent before starting the interview. With participants' consent, we audio-recorded and then transcribed the interviews.

Interviews lasted approximately 20 to 40 minutes. The interview was loosely structured and consisted of a series of open-ended questions. Questions were based on a list developed by the Health Technology Assessment International Interest Group on Patient and Citizen Involvement in Health Technology Assessment.[101] Questions focused on the impact of BPH, its impact on quality of life, and people's experiences with various treatment processes. Participants were also asked about their experiences with prostatic artery embolization, if applicable, including their perceptions of the benefits or limitations of this procedure and its impact. See Appendix 9 for our interview guide.

DATA EXTRACTION AND ANALYSIS

We used a modified version of a grounded-theory methodology to analyze interview transcripts. The grounded-theory approach allowed us to organize and compare information on experiences across participants. This method consists of a repetitive process of obtaining, documenting, and analyzing responses while simultaneously collecting, analyzing, and comparing information.[102,103] We used the qualitative data analysis software program NVivo[104] to identify and interpret patterns in the data. The patterns we identified allowed us to highlight the impact of BPH on quality of life and perceptions of prostatic artery embolization as a treatment for BPH.

Results

DIAGNOSIS AND IMPACT OF BPH

Benign prostatic hyperplasia is the enlargement of the prostate gland, a non-cancerous condition in people with prostates. During interviews, participants spoke of their diagnosis, the information they received from physicians about their enlarged prostate, and the formal diagnosis of BPH. Diagnosis can be made in several ways, including through bloodwork or the use of an ultrasound to scan the prostate gland.

> *They were using what they called a trans-rectal ultrasound. And…the result came up to say, "Yeah, you have BPH. It's in its early stages, but [the prostate is] very enlarged."*

This diagnosis often occurred after the participant noticed a number of symptoms associated with BPH. Symptoms of an enlarged prostate can include the frequent need to urinate, a weak or slow urine stream, bladder urgency, the inability to completely empty the bladder, and incontinence. During interviews, participants reported that these symptoms could occur for weeks or even months at a time.

> *I would go to the washroom probably three times a night. This is before. And it didn't bother me…I do a lot of work at night anyway.*

> *As I went [in]to my sixties…the need to void…became even greater, more often.*

> *My…symptoms started with basically, going back over 10, nearly 15, years, with a decrease in the stream, but not to the point of obstruction or any other symptoms, just a small stream.*

Participants reported that these symptoms and associated issues could negatively impact work responsibilities, social events, and other activities of daily living. Some reported having to reduce work hours or adjust their activities to accommodate their condition and the problems caused by the symptoms of BPH.

> *And that was particularly debilitating at work and meant, really, I couldn't travel.*

> *It was starting to really have an impact on my life. And then second to that was, it was clear that there was [a] further obstruction developing, because I had increasing [bladder] urgency.*

> *I would have periods that would last for a couple of weeks of frank bleeding when I urinated bright, then with clots. And this would occur spontaneously; it would occur after if I had been doing some heavy lifting or straining. I couldn't ride a bike because that would stimulate it. I couldn't exercise because that would stimulate it. So it was becoming very debilitating.*

As participants continued to suffer with an enlarged prostate, some spoke of the increasing severity of their symptoms, which included an increasing challenge of urination until it became impossible and a hospital visit was required for catheterization. Another participant reported on the development of hematuria.

> *All of a sudden, out of the clear, I couldn't go. I said to my wife, "I can't go; something's wrong." So I go in and I keep trying, and then spasms start like I've never seen in my life before…. Massive, massive bladder spasms. And I tried to go, and I couldn't. It was just awful."*

> *What progressed over the last 12 months has been recurrence of bleeding to the point where…it was unpredictable whether or not I would pass, have blood in my*

> *urine. And I'd go to a public urinal, and the next thing you know I'm passing blood…and it's just really embarrassing in that environment.*

For one individual, the enlarged prostate required long-term use of a catheter to allow for the flow of urine. This was a significant impediment to certain activities and negatively affected this individual's quality of life, requiring multiple visits to health care providers to resolve issues arising from catheter use.

> *It was 7 months I had the catheter. You're not supposed to have that. But I had no choice. I had a miserable time with it, very miserable. Why? Because it would block. And then I would have to go down to the hospital, wait 5 hours [for a health care provider to] drain me…because it would clog.*

CARE JOURNEYS

Once a diagnosis of BPH was made, participants reported similar medical pathways to treatment for their condition. Primarily, pharmacotherapy was attempted first to stabilize the growth of the prostate and potentially reduce the size of the gland. Medications could be taken for several months to try to achieve this outcome without surgery.

> *I told my doc, and he sent me to a specialist, and they gave me Rapiflow, 8 milligrams. Rapiflow is an alpha-drug, and it certainly stopped me going three times a night. I ended up going once, which was fine; everything was fine.*

Of those participants we interviewed, all but one had undergone PAE, so we expected the reported effectiveness of medications for treatment to be lower than it may be in the general population. This is a potential bias of our small sample size. One of the participants reported that the medications had unwanted side effects, which reduced his willingness to take them and also his satisfaction with his treatment.

> *These medications either weren't helping me or, in particular with the testosterone blocker, I was really getting mood changes. I was just finding it not…conducive to my quality of life and the way I was working, the way I had to work in [my job], so I wanted to come off those medications.*

Another participant reported receiving treatment for a potential infection, which was thought to be contributing to the enlarged prostate and inability to void.

> *[My doctor] thought that [there] may be an infection…He just said, "Maybe, let's try two weeks." So he pulled the catheter, out and I had to see if I voided. I couldn't. I tried desperately, and I couldn't. I tried everything, and I couldn't. I went back in to [my doctor, and he] inserted [the catheter] again, voided me, took the urine out.*

During the ongoing monitoring of BPH, each participant reported receiving ultrasounds to monitor the size, and several mentioned receiving biopsies as well, to check for any developing cancer in the prostate or other potential causes of the enlargement.

> *[I had a] PSA that was…about 10 times normal, so it was very elevated in the mid-teens, around 15 or 16. That stimulated a lot of evaluation from that point on,*

> *including numerous trans-rectal ultrasounds of the prostate, biopsies of the prostate on three or four occasions, including a fusion biopsy, which involved fusing an MRI and ultrasound to target the anterior lobe of the prostate.*
>
> *In a span of 10 years, in my sixties, I had three biopsies done on the prostate, and each time it came out, whatever they found was benign, [so I] don't need to worry.*
>
> *And what was seen on the ultrasound…and on direct cystoscopies was a very vascular gland. Once again, no tumour. I had a complete work-up of my urinary tract system, from the kidneys down, and there was no sign of any other pathology, so it was all coming from the prostate.*

DECISION-MAKING

Given the ineffectiveness, as reported by participants, of medications to reduce the size of their prostate, there was a desire to seek out a more permanent treatment to reduce the negative impact of their symptoms. Some participants mentioned conducting their own research and seeking out information themselves, including surgery. However, some participants reported feeling that surgery was too risky or was not an approach they wanted to follow. One participant mentioned incontinence as a potential side effect from surgery as a reason why that procedure was not desired.

> *I was looking for a…solution…. There was not a huge amount online to look at. Really. There were a few studies.*
>
> *I was disposed already to do research, so whenever something new came my way, I went and looked at it, and I don't know [about] now, but at that time the prostate surgery was [like] a turkey shoot or Russian roulette. So the negatives were far too many.*
>
> *At that time, the number one…side effect was impotence. And the problem still is that the area that they need to go with the scalpel is a nerve centre…There are a lot of nerve endings in that area. And if the person holding the scalpel…misses by less than a millimetre, you're done. You'd have incontinence for the rest of your life. And I did not look forward to being incontinent.*

In attempting to make a decision about the potential treatment options, all participants reported positively on the information and support they received from health care providers. Both family doctors and specialists provided valuable information and insight as to the potential benefits and drawbacks of different treatment options. Participants reported feeling comforted by the information and valued having a choice as to which potential treatment to choose.

> *They asked me what I wanted to do. And they gave me a choice: "Do you want to do the [PAE]?" And then they said, "If that doesn't work, we'll book you [for] a TURP."*
>
> *And I was fortunate that the urologist…he was the one [who] suggested it to me. I had not…pursued that [option (surgery)] myself. So, he was really thinking about alternative strategies for me, which I really liked.*

PROSTATIC ARTERY EMBOLIZATION

Three of the participants reported deciding (in consultation with their doctors) to undergo a PAE procedure to treat their enlarged prostate. Participants reported feeling well-informed ahead of time about the potential risks of the procedure. They also reported knowing that the procedure may not be completely successful.

> *[My doctor] told me about the procedure, what I needed to do, and he says…that it's probably [a] 75% chance of success. Okay.*
>
> *I [could determine] what the complications might be, and [I] knew that there was a potential risk of actually not being able to embolize the [prostatic] arteries, depending on the anatomy, but I was prepared to take all of that risk.*
>
> *The discussion was around whether or not to have another trans-urethral resection and…laser or prosthetic artery embolization. With the problem being bleeding…and that it had recurred despite the previous laser therapy, I thought that that [PAE] would be a good alternative for me.*

Additionally, some participants felt that other procedures to reduce the size of the prostate, such as TURP, were more invasive, dangerous, or had less chance of success and they therefore preferred PAE as a first attempt.

> *A TURP on a large prostate is dangerous. It's huge, and [the surgeon has to] scrape a lot [to] get it out…This one worked.*
>
> *[Prostatic artery embolization] also had the advantage of potentially shrinking down the prostate and helping my obstructive symptoms. So I saw the value in that, that's the first. The second, I wanted a procedure that was nowhere near as invasive as a TURP.*

Participants who underwent the PAE procedure described it in detail. Overall, the procedure was not seen as being too painful or burdensome, but it did have some uncomfortable aspects, including the need to remain still for a long period of time. Participants reported positive impressions of the staff and the overall processes to conduct the procedure.

> *For 2.5 hours I had to be still. I couldn't move. But it's okay, it was worthwhile. I waited, and then he delivered…the dye into five separate areas of the prostate.*
>
> *So, a day procedure…I have to say, the system of [the hospital] for doing this procedure was really very straightforward, and there were no hiccups. People knew what they were doing and what the procedure was. It was very well explained, so that was reassuring. And the procedure itself went very well; they allow around two to two and a half hours for it.*
>
> *It was done under very mild sedation, so there was no discomfort.*

Participants reported that the length of time for recovery was relatively short, with no need for a stay in hospital, and there were no serious side-effects. One participant reported feeling that he returned to work too quickly and that this may have negatively affected his recovery.

> *This [procedure] went [normally]; [in] next 2 hours I was walking, no problem. My wife picked me up, took me home.*
>
> *I had a recovery period of about 4 hours just to make sure that there were no problems associated with vascular access, and then [I] went home.*
>
> *I was anticipating [some soreness], but it was more just this discomfort that was in my pelvis. But it was actually very distracting…and I think I aggravated that possibly by going back to work and not giving it time to settle down. So, while they say that you'll be up and about quickly…you really do need to give yourself…a few days of rest.*

Overall, participants reported being very satisfied with the procedure and its effect on their symptoms. Participants who underwent PAE reported a decrease in symptoms, including a return to more regular urination and disappearance of hematuria. Participants also reported valuing the less invasive nature of the procedure and the lack of pain in recovery.

> *It was a wonderful experience, and I'm as happy as I can be. I'm clean, and it's a wonderful procedure, considering. Because [with] the pain from the other one, I'd be out for weeks.*
>
> *And from that day on, I peed beautifully and still until this day. Now the other thing is, generally I'm one or zero [times] going to the washroom at night. That's it. Most times it's zero, sometimes it's one. That's my story. And it's a wonderful procedure, and it's worked. And considering the size of my prostate and [that] this [procedure] worked, this is for anybody who needs it; this is a wonderful procedure.*
>
> *My urgency is very intermittent, but much, much, much less and is not a problem; [it's] easily managed. I'm sleeping through the night, my stream is good, and there's been absolutely no bleeding. So, in terms of response…I'm really pleased. It's just been such an important improvement in my quality of life and things that I can do.*

Interview participants who had received PAE reported that they were aware that the procedure was not a cure or complete fix for their condition. They were informed by their physicians that BPH could return and that their symptoms could return, requiring further intervention. This information did not decrease their satisfaction with the procedure as a treatment for their symptoms and for improving quality of life.

> *They generally think that I have 7 years [of symptom relief]…so I'm now 1 year, but I still haven't picked up; [my prostate is] still at 100 mL; it hasn't grown at all. So I'm just telling you this is a wonderful, wonderful procedure.*
>
> *The expectation is [to] monitor it for now and that it's unknown what the duration of this will be, because new blood vessels will grow. But they'll be different; they won't be the same sort of anatomic vessels. And so, my understanding is that…the*

> *procedure's going to…give me five years, possibly more, of relief. [But] it's not the final…outcome; [it] may not be the final procedure that I need.*

Discussion

Results for patient preferences and values surrounding the use of PAE treatment for BPH were relatively modest. Recruitment of patients for this assessment was challenging and limited by a lack of existing patient support groups for BPH and the limited clinical availability of the PAE procedure across the province. This limited access created a geographical recruitment bias in that all participants were located in southern Ontario or Ottawa; thus, their experiences may not fully reflect patient preferences and values from all areas of Ontario.

All participants spoke extensively about the symptoms of BPH and the impact of BPH on their daily activities, including sleep patterns and ability to work. Additionally, participants had researched and considered a number of treatment methods, allowing for valuable insight into decision-making and choosing to undergo the PAE procedure.

Participants reported consistent positive impressions of the PAE procedure and its ability to reduce their symptoms of BPH and improve quality of life.

Conclusions

Enlargement of the prostate gland attributed to BPH can cause a number of symptoms that can negatively affect an individual's quality of life. Participants reported on these negative impacts and the perceived positive result of treating their BPH with PAE. Information and discussions with physicians about different treatment options were valued by participants and helped in their decision-making regarding whether to undergo PAE. Participants valued that PAE was less invasive and reported that the procedure led to a reduction of their BPH symptoms. Participants consistently described positive impressions of the PAE procedure and feel their lives have been improved by it, despite knowing that the results may not be permanent.

Conclusions of the Health Technology Assessment

We found limited comparative evidence on the effectiveness and safety of prostatic artery embolization (PAE) for benign prostatic hyperplasia (BPH), especially in the long term (beyond 1 year). We only found studies comparing PAE with transurethral resection of the prostate (TURP) or open simple prostatectomy (OSP). Prostatic artery embolization may improve BPH symptoms and urodynamic measures, but we are uncertain if the procedure results in similar outcomes as those of TURP (GRADE: Very low to Low). Compared with TURP, PAE may result in higher patient satisfaction (GRADE: Not assessed). Based on one observational study, PAE may result in smaller improvements compared with OSP, but we are very uncertain of the evidence (GRADE: Very low). Compared with TURP or OSP, PAE may result in fewer adverse events (GRADE: Not assessed).

The economic evidence on PAE is limited. We did not identify any cost-effectiveness studies comparing PAE with alternative treatments for BPH. We did, however, identify three costing studies (including one in Ontario) that showed PAE to be less costly than TURP from the hospital perspective. Our primary economic evaluation found that, compared with TURP, PAE is more costly but it does have a small QALY increase due to fewer adverse events. Compared with OSP, PAE is less costly and less effective. Overall, PAE is unlikely to be cost-effective. Publicly funding PAE in people with BPH would lead to an additional cost of $11,400 over the next 5 years.

People we spoke with who had lived experience with BPH reported that it caused a number of symptoms that negatively affected their quality of life. Those who had the PAE procedure found it to be less invasive and successful in reducing symptoms and improving their quality of life. Their impressions of PAE were positive, despite knowing that the results may not be permanent.

Abbreviations

BPH	Benign prostatic hyperplasia
CADTH	Canadian Agency for Drugs and Technologies in Health
CI	Confidence interval
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
ICER	incremental cost-effectiveness ratio
IIEF	International Index of Erectile Function
IPSS	International Prostate Symptom Score
OHIP	Ontario Health Insurance Plan
OSP	Open simple prostatectomy
PAE	Prostatic artery embolization
PErFecTED	Proximal embolization first then embolize distal method of prostatic artery embolization
PSA	Prostate-specific antigen
PVP	photoselective vaporization
QALY	quality-adjusted life-year
RCT	Randomized controlled trial
TUR	Transurethral resection
TURP	Transurethral resection of the prostate

Glossary

Adverse event	An adverse event is an unexpected medical problem that happens during treatment for a health condition. Adverse events may be caused by something other than the treatment.
Budget impact analysis	A budget impact analysis estimates the financial impact of adopting a new health care intervention on the current budget (i.e., the affordability of the new intervention). It is based on predictions of how changes in the intervention mix will impact the level of health care spending for a specific population. Budget impact analyses are typically conducted for a short-term period (e.g., 5 years). The budget impact, sometimes referred to as the net budget impact, is the estimated cost difference between the current scenario (i.e., the anticipated amount of spending for a specific population without using the new intervention) and the new scenario (i.e., the anticipated amount of spending for a specific population following the introduction of the new intervention).
Cost–benefit analysis	A cost–benefit analysis is a type of economic evaluation that expresses the effects of a health care intervention in terms of a monetary value so that these effects can be compared with costs. Results can be reported either as a ratio of costs to benefits or as a simple sum that represents the net benefit (or net loss) of one intervention over another. The monetary valuation of the different intervention effects is based on either prices that are revealed by markets or an individual or societal willingness-to-pay value.
Cost–consequence analysis	A cost–consequence analysis is a type of economic evaluation that estimates the costs and consequences (i.e., the health outcomes) of two or more health care interventions. In this type of analysis, the costs are presented separately from the consequences.
Cost-effective	A health care intervention is considered cost-effective when it provides additional benefits, compared with relevant alternatives, at an additional cost that is acceptable to a decision-maker based on the maximum willingness-to-pay value.
Cost-effectiveness acceptability curve	In economic evaluations, a cost-effectiveness acceptability curve is a graphical representation of the results of a probabilistic sensitivity analysis. It illustrates the probability of health care interventions being cost-effective over a range of willingness-to-pay values. Willingness-to-pay values are plotted on the horizontal axis of the graph, and the probability of the intervention of interest and its comparator(s) being cost-effective at corresponding willingness-to-pay values is plotted on the vertical axis.

Cost-effectiveness analysis	Used broadly, "cost-effectiveness analysis" may refer to an economic evaluation used to compare the benefits of two or more health care interventions with their costs. It may encompass several types of analysis (e.g., cost-effectiveness analysis, cost–utility analysis). Used more specifically, "cost-effectiveness analysis" may refer to a type of economic evaluation in which the main outcome measure is the incremental cost per natural unit of health (e.g., life-year, symptom-free day) gained.
Cost-effectiveness plane	In economic evaluations, a cost-effectiveness plane is a graph used to show the differences in cost and effectiveness between a health care intervention and its comparator(s). Differences in effects are plotted on the horizontal axis, and differences in costs are plotted on the vertical axis.
Cost–utility analysis	A cost–utility analysis is a type of economic evaluation used to compare the benefits of two or more health care interventions with their costs. The benefits are measured using quality-adjusted life-years, which capture both the quality and quantity of life. In a cost–utility analysis, the main outcome measure is the incremental cost per quality-adjusted life-year gained.
Discounting	Discounting is a method used in economic evaluations to adjust for the differential timing of the costs incurred and the benefits generated by a health care intervention over time. Discounting reflects the concept of positive time preference, whereby future costs and benefits are reduced to reflect their present value. The health technology assessments conducted by Ontario Health (Quality) use an annual discount rate of 1.5% for both future costs and future benefits.
Disutility	A disutility is a decrease in utility (i.e., a decrease in preference for a particular health outcome) typically resulting from a particular health condition (e.g., experiencing a symptom or complication).
Dominant	A health care intervention is considered dominant when it is more effective and less costly than its comparator(s).
Health-related quality of life	Health-related quality of life is a measure of the impact of a health care intervention on a person's health. It includes the dimensions of physiology, function, social life, cognition, emotions, sleep and rest, energy and vitality, health perception, and general life satisfaction.
Health state	A health state is a particular status of health (e.g., sick, well, dead). A health state is associated with some amount of benefit and may be associated with specific costs. Benefit is captured through individual or societal preferences for the time spent in each health state and is expressed in quality-adjusted weights called utility values.
Incremental cost	The incremental cost is the additional cost, typically per person, of a health care intervention versus a comparator.

Incremental cost-effectiveness ratio (ICER)	The incremental cost-effectiveness ratio (ICER) is a summary measure that indicates, for a given health care intervention, how much more a health care consumer must pay to get an additional unit of benefit relative to an alternative intervention. It is obtained by dividing the incremental cost by the incremental effectiveness. Incremental cost-effectiveness ratios are typically presented as the cost per life-year gained or the cost per quality-adjusted life-year gained.
Microsimulation model	In economic evaluations, a microsimulation model (e.g., an individual-level or patient-level model) is used to simulate the health outcomes for a heterogeneous group of patients (e.g., patients of different ages or with different sets of risk factors) after receiving a particular health care intervention. The health outcomes and health events of each patient are modelled, and the outcomes of several patients are combined to estimate the average costs and benefits accrued by a group of patients. In contrast, a cohort model follows a homogeneous cohort of patients (e.g., patients of the same age or with the same set of risk factors) through the model and estimates the proportion of the cohort who will experience specific health events.
Ministry of Health perspective	The perspective adopted in economic evaluations determines the types of costs and health benefits to include. Ontario Health (Quality) develops health technology assessment reports from the perspective of the Ontario Ministry of Health. This perspective includes all costs and health benefits attributable to the Ministry of Health, such as treatment costs (e.g., drugs, administration, monitoring, hospital stays) and costs associated with managing adverse events caused by treatments. This perspective does not include out-of-pocket costs incurred by patients related to obtaining care (e.g., transportation) or loss of productivity (e.g., absenteeism).
Monte Carlo simulation	Monte Carlo simulation is an economic modelling method that derives parameter values from distributions rather than fixed values. The model is run several times, and in each iteration, parameter values are drawn from specified distributions. This method is used in microsimulation models and probabilistic sensitivity analysis.
Natural history of a disease	The natural history of a disease is the progression of a disease over time in the absence of any health care intervention.
Probabilistic sensitivity analysis	A probabilistic sensitivity analysis is used in economic models to explore uncertainty in several parameters simultaneously and is done using Monte Carlo simulation. Model inputs are defined as a distribution of possible values. In each iteration, model inputs are obtained by randomly sampling from each distribution, and a single estimate of cost and effectiveness is generated. This process is repeated many times (e.g., 10,000 times) to estimate the number of times (i.e., the probability) that the health care intervention of interest is cost-effective.

Quality-adjusted life-year (QALY)	The quality-adjusted life-year (QALY) is a generic health outcome measure commonly used in cost–utility analyses to reflect the quantity and quality of life-years lived. The life-years lived are adjusted for quality of life using individual or societal preferences (i.e., utility values) for being in a particular health state. One year of perfect health is represented by one quality-adjusted life-year.
Reference case	The reference case is a preferred set of methods and principles that provide the guidelines for economic evaluations. Its purpose is to standardize the approach of conducting and reporting economic evaluations, so that results can be compared across studies.
Scenario analysis	A scenario analysis is used to explore uncertainty in the results of an economic evaluation. It is done by observing the potential impact of different scenarios on the cost-effectiveness of a health care intervention. Scenario analyses include varying structural assumptions from the reference case.
Sensitivity analysis	Every economic evaluation contains some degree of uncertainty, and results can vary depending on the values taken by key parameters and the assumptions made. Sensitivity analysis allows these factors to be varied and shows the impact of these variations on the results of the evaluation. There are various types of sensitivity analysis, including deterministic, probabilistic, and scenario.
Time horizon	In economic evaluations, the time horizon is the time frame over which costs and benefits are examined and calculated. The relevant time horizon is chosen based on the nature of the disease and health care intervention being assessed, as well as the purpose of the analysis. For instance, a lifetime horizon would be chosen to capture the long-term health and cost consequences over a patient's lifetime.
Utility	A utility is a value that represents a person's preference for various health states. Typically, utility values are anchored at 0 (death) and 1 (perfect health). In some scoring systems, a negative utility value indicates a state of health valued as being worse than death. Utility values can be aggregated over time to derive quality-adjusted life-years, a common outcome measure in economic evaluations.
Willingness-to-pay value	A willingness-to-pay value is the monetary value a health care consumer is willing to pay for added health benefits. When conducting a cost–utility analysis, the willingness-to-pay value represents the cost a consumer is willing to pay for an additional quality-adjusted life-year. If the incremental cost-effectiveness ratio is less than the willingness-to-pay value, the health care intervention of interest is considered cost-effective. If the incremental cost-effectiveness ratio is more than the willingness-to-pay value, the intervention is considered not to be cost-effective.

Appendix 1: Guideline Recommendations on Prostatic Artery Embolization

Table A1: Guideline Recommendations on Prostatic Artery Embolization

Author, Year	Recommendation (Verbatim)
Canadian Guidelines	
Canadian Urology Association, 2018[6]	We recommend that PAE should not be offered at this time for the treatment of LUTS due to BPH (conditional recommendation based on moderate-quality evidence).
International Guidelines	
German Society for Interventional Radiology, 2020[23]	• PAE, an endovascular procedure, is a patient-friendly, minimally invasive, alternative therapy option of the benign prostate syndrome • PAE can reduce the symptoms of the LUTS, comparable to transurethral resection TUR. The deobstructive and volume-reducing potential of the PAE is inferior to that of the TUR • The main advantages of PAE are use of local anesthesia (no general anesthesia required), short patient recovery, and maintenance of sexual function, including antegrade ejaculation • Based on current evidence, PAE should be considered after conservative drug therapy and before TUR • The role of PAE in the context of other minimally invasive procedures requires further evaluation with an open-minded approach towards PAE • PAE is carried out by interventional radiologists, usually on a referral basis from urologists, and requires close interdisciplinary cooperation
American Urological Association, 2020[21]	PAE for the treatment of LUTS secondary to BPH is not supported by current data and trial designs, and benefit over risk remains unclear; therefore, PAE is not recommended outside the context of clinical trials (expert opinion).
Cardiovascular and Interventional Radiological Society of Europe, 2019[26]	Indications • Patients with moderate to severe LUTS related to BPH may benefit from prostatic artery PAE (level of evidence: 1a; evidence from systematic review or meta-analysis of RCTs) • PAE can be performed in patients with symptomatic BPH, in case of failure of medical treatment (level of evidence: 1a; evidence from systematic review or meta-analysis of RCTs) • PAE can be performed in patients suffering from urinary retention due to BPH without an upper limit of prostate size (level of evidence: 1b; evidence from at least 1 RCT) • PAE can be performed in patients who have comorbidities (for instance, patients using anticoagulation or antiplatelet therapy) (level of evidence: 2b; individual retrospective cohort study or low-quality RCT) • PAE is suited to younger, sexually active patients who have concerns about retrograde ejaculation, erectile dysfunction, or urinary incontinence (level of evidence: 2b; individual retrospective cohort study or low-quality RCT) • PAE may be performed in patients with BPH and acute or chronic urinary retention in the setting of preserved bladder function as a method of achieving catheter independence (level of evidence: 2b; individual retrospective cohort study or low-quality RCT) • PAE may achieve cessation of bleeding in patients with haematuria of prostatic origin (level of evidence: 2b; individual retrospective cohort study or low-quality RCT) Preoperative scores and testing • IPSS and urodynamic testing provide a broad measure of the severity of symptoms of BPH. Inclusion criteria for PAE are: IPSS ≥ 8 and/or QOL score ≥ 3; prostate volume > 30–50 mL; a urine peak flow < 15 mL/s; post-void residual volume < 200 mL (level of evidence: 1a; evidence from systematic review or meta-analysis of RCTs)

Contraindications

- Relative contraindications to PAE are patients with bladder diverticuli size > 2 cm, bladder stone, detrusor hyperactivity or hypocontractility, neurogenic bladder and severe renal insufficiency (level of evidence: 1a; evidence from systematic review or meta-analysis of RCTs)
- In case of PSA level > 4 ng/ml, prostate biopsies must be discussed before the procedure with the referring urologist (level of evidence: 1a; evidence from systematic review or meta-analysis of RCTs)

Imaging

- Imaging by ultrasound, CTA and MRI can be used in combination to assess: prostate volume and post-void residual; vessel patency/course and collaterals; and serve as the baseline for follow-up, respectively (level of evidence: 1a; evidence from systematic review or meta-analysis of RCTs)
- Pre-operative imaging with a pelvic MRI and/or CTA or MR angiography scan may assess pelvic vasculature (level of evidence: 2b; individual retrospective cohort study or low-quality RCT)

Patient preparation, procedural features and variations of the technique of PAE

- Antibiotics (ciprofloxacin or cefazoline) can be used due to the risk of urinary tract infection, as in any prostate intervention (level of evidence: 5; evidence from a panel of experts)
- Although femoral approach is more often performed, transradial arterial access represents a safe and feasible method for performing PAE (level of evidence: 2a; systematic reviews [with homogeneity] of retrospective cohort studies)
- Cone-beam CT angiography may be used to identify the anatomical vascular anatomy of the prostate (level of evidence: 2a; systematic reviews [with homogeneity] of retrospective cohort studies)
- Digital subtraction angiography work-up allows visualisation of the prostate arteries and the characteristic blush of the prostate (level of evidence: 2a; systematic reviews [with homogeneity] of retrospective cohort studies)
- If anastomoses with pelvic arteries occur, proximal closure of the anastomoses can be performed using coils to avoid non-target embolization (level of evidence: 2a; systematic reviews [with homogeneity] of retrospective cohort studies)
- Slow-flow injection of highly diluted (20–40 mL solution) calibrated microspheres (300–500 µm) or polyvinyl alcohol particles (100–300 µm) is performed with a complete occlusion as endpoint (level of evidence: 2a; systematic reviews [with homogeneity] of retrospective cohort studies)
- The procedure is considered successful if at least 1 hemi-prostate is embolized, but in the vast majority of cases, both sides are embolized (level of evidence: 1a; evidence from systematic review or meta-analysis of RCTs)
- PErFectED (Proximal Embolization First, Then Embolize Distal) technique and balloon occlusion PAE may be used as options to secure prostate arterial occlusion (level of evidence: 3b; individual case–control study)

Medication and periprocedural care

- PAE is usually performed under local anaesthesia as an outpatient intervention (level of evidence: 1a; evidence from systematic review or meta-analysis of RCTs)
- Pain is infrequently reported and is controlled with oral medication (level of evidence: 2a; systematic reviews [with homogeneity] of retrospective cohort studies)
- Patients are usually discharged 3–6 h post-procedure (level of evidence: 2a; systematic reviews [with homogeneity] of retrospective cohort studies)

Outcomes

- Clinical follow-up is performed at 3, 6 and 12 months, including IPSS, IIEF and patient-reported complication domains (level of evidence: 1a; evidence from systematic review or meta-analysis of RCTs)
- Criteria of symptomatic improvement are defined by an IPSS < 18 with a decrease of at least 25% and a QOL score ≤ 3, with at least 1 point decrease, compared to baseline (level of evidence: 2b; individual retrospective cohort study or low-quality RCT)
- Clinical failure of the procedure is defined as the persistence of severe symptoms (IPSS decrease ≤ 25%, IPSS score ≥ 18, QOL score decrease ≤ 1, and a QOL score ≥ 4), or a decrease in the peak urinary

	flow (level of evidence: 2b; individual retrospective cohort study or low-quality RCT) In reporting adverse events following PAE, it is recommended to use the modified Clavien classification (level of evidence: 1a; evidence from systematic review or meta-analysis of RCTs)
Society of Interventional Radiology, Cardiovascular and Interventional Radiological Society of Europe, Société Française de Radiologie, British Society of Interventional Radiology, 2019[22,a]	• PAE is an acceptable minimally invasive treatment option for appropriately selected men with BPH and moderate to severe LUTS (level of evidence: moderate quality–randomized study design; strength of recommendation: strong) • PAE can be considered as a treatment option in patients with BPH and moderate to severe LUTS who have very large prostate glands (> 80 cm^3), without an upper limit of prostate size (level of evidence: moderate quality–nonrandomized study design; strength of recommendation: moderate) • PAE can be considered as a treatment option in patients with BPH and acute or chronic urinary retention in the setting of preserved bladder function as a method of achieving catheter independence (level of evidence: moderate quality–nonrandomized study design; strength of recommendation: moderate) • PAE can be considered as a treatment option in patients with BPH and moderate to severe LUTS who wish to preserve erectile and/or ejaculatory function (level of evidence: moderate quality–nonrandomized study design; strength of recommendation: weak) • PAE can be considered in patients with hematuria of prostatic origin as a method of achieving cessation of bleeding (level of evidence: limited quality; strength of recommendation: strong) • PAE can be considered as a treatment option in patients with BPH and moderate to severe LUTS who are deemed not to be surgical candidates for any of the following reasons: advanced age, multiple comorbidities, coagulopathy, or inability to stop anticoagulation or antiplatelet therapy (level of evidence: expert opinion; strength of recommendation: moderate) • PAE should be included in the individualized patient-centered discussion regarding treatment options for BPH with LUTS (level of evidence: expert opinion; strength of recommendation: strong) • Interventional radiologists, given their knowledge of arterial anatomy, advanced microcatheter techniques, and expertise in embolization procedures, are the specialists best suited for the performance of PAE (level of evidence: expert opinion; strength of recommendation: strong)
European Association of Urology, 2020[25]	Recommendations • Offer PAE to men with moderate to severe LUTS who wish to consider minimally invasive treatment options and accept less optimal objective outcomes compared with TURP (strength of recommendation: weak) • Perform PAE only in units where the work up and follow up is performed by urologists working collaboratively with trained interventional radiologists for the identification of PAE-suitable patients (strength of recommendation: strong) Note: PAE remains under investigation Summary of evidence for PAE • PAE is less effective than TURP at improving symptoms and urodynamic parameters such as flow rate (level of evidence: 1a) • Procedural time is longer for PAE compared to TURP, but blood loss, catheterization, and hospitalization time are in favour of PAE: 1b Practical considerations for PAE: a multidisciplinary team approach of urologists and radiologists is mandatory and patient selection should be done by urologists and interventional radiologists. The investigation of patients with LUTS to indicate suitability for invasive techniques should be performed by urologists only. This technically demanding procedure should only be done by an interventional radiologist with specific mentored training and expertise in PAE. Patients with larger prostates (> 80 mL) may have the most to gain from PAE. The selection of LUTS patients who will benefit from PAE still needs to be better defined. Further data with medium- and long-term follow-up are still required and comparison with other minimally invasive techniques would be valuable. However, current evidence of safety and efficacy of PAE appears adequate to support the use of this procedure for men with moderate to severe LUTS provided proper arrangements for consent and audit are in place; therefore, a

	recommendation has been given, but PAE remains under investigation.
National Institute for Health and Care Excellence, 2018[24]	• Current evidence on the safety and efficacy of PAE for BPH is adequate to support the use of this procedure provided that standard arrangements are in place for clinical governance, consent, and audit • Patient selection should be done by a urologist and an interventional radiologist • This technically demanding procedure should only be done by an interventional radiologist with specific training and expertise in PAE

Abbreviations: BPH, benign prostatic hyperplasia; CT, computed tomography; CTA, computed tomography angiography; IIEF, International Index of Erectile Function; IPSS, International Prostate Symptom Score; LUTS, lower urinary tract symptoms; MR, magnetic resonance; MRI, magnetic resonance imaging; PAE, prostatic artery embolization; PSA, prostate-specific antigen; QOL, quality of life; RCT, randomized controlled trial; TUR, transurethral resection; TURP, TUR of the prostate.

[a]Endorsed by the Asia Pacific Society of Cardiovascular and Interventional Radiology, Canadian Association for Interventional Radiology, Chinese College of Interventionalists, Interventional Radiology Society of Australasia, Japanese Society of Interventional Radiology, and Korean Society of Interventional Radiology.

Appendix 2: Summary of Published Systematic Reviews on Prostatic Artery Embolization

Table A2: Summary of Published Systematic Reviews on Prostatic Artery Embolization

Author, Year	Search Period	Databases	Inclusion Criteria	Critical Appraisal	No. Included Studies	Main Conclusions
Cizman et al, 2016[75]	Up to May 2015	PubMed, study reference lists	**Inclusion:** original research on PAE for LUTS due to BPH, > 3 participants, English language, ≥ 6 months of follow-up data **Exclusion:** reviews, letters, comments, conference abstracts	Adaptation of STROBE checklist and QUADAS-2	7 studies (1 RCT, 6 observational)	• Decreased IPSS, QOL, PVR, PSA level at 6 mo for PAE Increased Q_{max} at 6 mo for PAE • No difference in IPSS, QOL, PVR, PSA level, Q_{max} from 6 to 12 mo • Decrease in PV at 12 mo for PAE
Feng et al, 2017[105]	Up to April 2016	PubMed, Embase, CDSR, Web of Science, study reference lists	**Inclusion:** PAE for moderate to severe LUTS due to BPH, pre- and post-PAE results for outcomes of interest, English or Chinese language **Exclusion:** reviews, letters, editorials, comments, studies with insufficient data, studies with duplicate data from the same patients, studies of people with another suspected condition (not BPH)	Used previous systematic review's risk of bias assessment (Schreuder et al, 2014[106])	20 studies (14 prospective, 6 retrospective)	• Statistically significant improvements for PAE for IPSS, QOL, PSA level, PV, Q_{max}, and PVR • No significant difference in IIEF • Major complications after PAE mainly include pain in the perineum, retropubic area and/or urethra, and hematuria
Jiang et al, 2019[107]	May 1998 to May 2018	PubMed, Embase, CENTRAL	**Inclusion:** comparative studies of PAE vs. TURP for BPH, > 12-mo follow-up, includes at least one outcome of interest, English language **Exclusion**: case reports, reviews, editorials, comments, conference abstracts, articles with no outcomes of interest, studies with insufficient data, noncomparative studies	Cochrane Risk of Bias tool for RCTs Newcastle-Ottawa Scale for observational studies	4 comparative studies (2 RCTs, 2 observational)	• Q_{max} was higher with TURP than PAE • Postoperative QOL was lower with TURP than PAE • Postoperative PV was significantly smaller with TURP than PAE • Operative time was significantly shorter with TURP than PAE • No significant difference was found for postoperative IPSS and complications between TURP and PAE
Kuang et al, 2017[108]	Up to August 2015	MEDLINE, Embase, Cochrane Library, Web of	**Inclusion:** PAE for symptomatic BPH, peer-reviewed, ≥ 10 participants, at least one outcome of interest, with ≥ 1 mo follow-up **Exclusion:** studies unrelated to PAE	OCEBM levels of evidence	10 studies (1 RCT, 9 observational)	• PAE is effective for LUTS due to BPH in the short- and intermediate-term • At 6 mo, PV, PVR, Q_{max}, IPSS, and QOL were significantly improved

Author, Year	Search Period	Databases	Inclusion Criteria	Critical Appraisal	No. Included Studies	Main Conclusions
		Science	or BPH, studies with < 10 participants, reviews, letters, editorials, animal/non-human studies, conference abstracts, studies with overlapping data			• No significant change for PSA levels • At 12 and 24 mo, PV, PSA, PVR, Q_{max}, IPSS, and QOL were significantly improved
Lebdai et al, 2015[109]	January 2008 to January 2015	PubMed, MEDLINE, study reference lists	**Inclusion:** people with LUTS due to benign prostatic obstruction **Exclusion:** reviews, editorials, animal studies, PAE for indications other than BPH, studies with < 30 participants or with overlaps in data collection	Not reported	4 studies (1 RCT, 3 noncomparative)	• PAE showed significantly lower IPSS reduction at 1 and 3 mo vs. TURP • Similar trend was seen from 6 to 24 mo, but improvements were not significant • Major complications were rare • Mild adverse events occurred in 10% of people • Further comparative studies are needed
Li et al, 2019[110]	January 1, 2000, to June 30, 2017	PubMed, MEDLINE, Embase, Cochrane Library	PAE for LUTS/BPH Study design: RCTs	Cochrane risk of bias	9 retrospective studies	• QOL scores were significantly lower after PAE at 1, 3, and 12 mo • No significant change after PAE for at 1 and 3 mo, but significant decrease at 12 mo • Significant improvements for IPSS, Q_{max}, and PVR after PAE at 1, 3, and 12 mo • Significant improvement in PSA at 3 mo only (no change at 1 and 12 mo) • No significant improvements in IIEF-5 after PAE at 1, 3, and 12 mo • PAE is an effective treatment for BPH-induced LUTS
Malling et al, 2019[111]	Up to March 22, 2017	PubMed, Web of Science, Cochrane Library, Embase	**Inclusion:** studies on the efficacy of PAE for BPH, any language **Exclusion:** studies with < 10 participants, < 6 mo follow-up, PAE for indications other than BPH, conference papers, case reports,	Cochrane risk of bias tool for RCTs	13 studies (2 RCTs, 8 prospective noncomparative, 3 retrospective)	• Significant improvements in all outcomes at 12 mo • Low complication rate (0.3%) • PAE can reduce moderate to severe LUTS in people with BPH with a low risk

Author, Year	Search Period	Databases	Inclusion Criteria	Critical Appraisal	No. Included Studies	Main Conclusions
			abstracts			of complications
Pyo and Cho, 2017[112]	Up to December 2015	PubMed, MEDLINE, study reference lists	**Inclusion:** PAE for people with BPH, included follow-up results, English language, full-text article	Cochrane risk of bias tool	7 studies (2 RCTs, 5 observational)	• PAE may improve LUTS at short- and mid-term follow-up • More comparative studies are needed and studies with long-term follow-up
Schreuder et al, 2014[106]	Up to November 2013	MEDLINE, Embase	**Inclusion:** studies with > 5 people who had PAE for BPH, included one or more outcomes of interest **Exclusion:** duplicates, reviews, comments, letters, case reports (< 5 participants), studies not on BPH, animal studies, conference abstracts, nonhuman studies	Based on QUADAS-2	9 studies (1 RCT comparing different PVA particle sizes, 1 observational comparing unilateral vs. bilateral embolization, 7 noncomparative observational)	• Decrease in PV and PVR was mainly in the first month after PAE, with further decrease up to 12 mo, but then increasing after • PSA levels decrease up to 3 mo after PAE, but then increasing after • Q_{max} increased mainly in the first month and decreased after 30 mo • IPSS and QOL improved mainly in the first month, with further improvement up to 30 mo • No change in IIEF after PAE • PAE procedure seems safe
Shim et al, 2017[113]	Up to January 2016	MEDLINE, Cochrane Library	**Inclusion:** PAE for BPH, reasonable ITT analysis for RCTs and clinical trials, prospective studies	Cochrane risk of bias tool; GRADE for outcomes	16 studies (3 comparative RCTs, 13 noncomparative)	• PAE efficacy is inferior to standard treatment methods • Persistence of improvements cannot be guaranteed • PAE should still be considered experimental
Teoh et al, 2017[114]	Up to May 1, 2016	PubMed, EMBASE, Web of Science	**Study design:** RCTs, comparative observational studies **Inclusion:** full-length research articles, conference abstracts, any language on PAE **Exclusion:** single-arm studies, case series, case reports, non-human studies	Jadad Scale for RCTs Newcastle-Ottawa Scale for observational studies	5 studies (2 RCTs, 3 comparative observational)	• TURP had better IPSS than PAE • Open prostatectomy had better IPSS, QOL, Q_{max}, PVR, but worse IIEF than PAE at 1 y • Unilateral PAE had higher rate of poor clinical outcome than bilateral PAE, but the difference was nonsignificant after adjusting for age • No difference in IPSS, QOL, Q_{max}, PVR, IIEF, PV, and PSA level

Author, Year	Search Period	Databases	Inclusion Criteria	Critical Appraisal	No. Included Studies	Main Conclusions
						• PAE with 100 µm PVA particles had greater reduction in PSA level, but worse IIEF vs. 200 µm PVA particles • No difference in IPSS, QOL, Q_{max}, PVR, PV, and poor clinical outcome • Further comparative studies are needed
Uflacker et al, 2016[115]	November 2009 to October 2015	MEDLINE, NCBI	**Inclusion:** PAE for the treatment of LUTS, English language, published literature, case reports only for complications **Exclusion:** commentaries, non-peer-reviewed data, conference abstracts, reviews, letters, case reports for effectiveness	Based on PRISMA guidelines and previously published SRs (Schreuder et al, 2014[106] and Cizman et al, 2016[75])	6 noncomparative studies	• Improved Q_{max}, PVR, IPSS, and QOL at 12 mo • No adverse effect on erectile function • Low incidence of serious adverse events, but minor adverse events were common
Vreugdenburg and Wild (Ludwig Boltzmann Institut), 2017[18]	Up to December 9, 2016	MEDLINE, Embase, Cochrane Library, CRD, study reference lists	**Study design:** RCTs and observational studies **Inclusion:** English or German language studies on PAE	AMSTAR for SRs Cochrane risk of bias tool for RCTs ROBINS-I for nonRCTs IHE checklist for case series GRADE for outcomes	9 studies (3 RCTs, 2 observational, 2 case series)	• Overall strength of evidence for the effectiveness of PAE vs. TURP is low • Strength of evidence for the effectiveness of PAE vs. open prostatectomy is moderate • Strength of evidence for the safety of PAE vs. TURP or open prostatectomy is moderate
Wang et al, 2016[48]	1980 to 2016	MEDLINE, Embase, CENTRAL, study reference lists	**Inclusion:** PAE for BPH, studies with data on outcomes of interest, studies where full text could be retrieved	Newcastle-Ottawa Scale	12 noncomparative studies (10 prospective, 2 retrospective)	• PAE is an effective and safe treatment for LUTS related to BPH Studies with larger numbers of participants and longer follow-up times are needed
Williams and Ryce (Canadian Agency for Drugs and Technologies in Health),	January 1, 2016, to July 29, 2019	PubMed, Cochrane Library, CRD, websites of Canadian and major international	**Study design:** HTAs, SRs, meta-analyses, RCTs, observational studies **Inclusion:** People with BPH who have LUTS	AMSTAR 2 for SRs Downs and Black checklist for comparative studies	2 SRs and 1 observational study	• Results comparing PAE vs. TURP were mixed, with some outcomes favouring PAE while others favoured TURP • In general, PAE was safer than TURP

Author, Year	Search Period	Databases	Inclusion Criteria	Critical Appraisal	No. Included Studies	Main Conclusions
2019[116]		health technology agencies, focused Internet search				
Xu et al, 2019[117]	Inception to June 2019	Web of Science, PubMed, Embase, Cochrane Library, clinicaltrials.gov, CNKI, Wanfang, VIP databases, reference lists of SRs and meta-analyses	**Study design:** RCTs and comparative observational studies **Inclusion:** People with BPH **Exclusion:** noncomparative studies, reviews, comments, recommendations, letters, ongoing trials, protocols, abstracts, consensus or statements, studies with incomplete data or no data of interest	Revised Jadad composite scale	9 studies (4 RCTs, 5 observational)	• PAE was inferior to TURP for IPSS, QOL, PV, Q_{max} • TURP still the gold standard, but PAE may be a valuable alternative to TURP in the treatment of BPH patients who refuse surgery or who have surgery contraindications
Zumstein et al, 2018[19]	Up to June 23, 2018	MEDLINE, Embase, CRD, study reference lists	**Study design:** RCTs, quasi-RCTs, comparative observational studies **Inclusion: s**tudies on PAE vs. standard surgical procedures for BPH	Cochrane risk of bias tool for RCTs ROBINS-I for observational studies GRADE for outcomes	5 studies (3 RCTs, 2 observational)	• Moderate-quality evidence for PAE in the short-term • PAE showed significant advantages for safety and sexual function, but clear disadvantages for all other patient-reported and functional outcomes • Further RCTs with longer follow-up periods are needed to evaluate the mid- and long-term effectiveness and safety of PAE

Abbreviations: AMSTAR, A Measurement Tool to Assess Systematic Reviews; BPH, benign prostatic hyperplasia; CDSR, Cochrane Database of Systematic Reviews; CNKI, China National Knowledge Infrastructure; CRD, University of York Centre for Reviews and Dissemination; IIEF, International Index of Erectile Function; IPSS, International Prostate Symptom Score; ITT, intention-to-treat, LUTS, lower urinary tract symptoms; OCEBM, Oxford Centre for Evidence-based Medicine; PAE, prostatic artery embolization; PSA, prostate-specific antigen; PV, prostate volume; PVR, post-void residual; QOL, quality of life; Q_{max}, maximum (peak) urinary flow; QUADAS, Quality Assessment of Diagnostic Accuracy Studies; RCT, randomized controlled trial; SR, systematic review; STROBE, Strengthening the Reporting of Observational studies in Epidemiology; TURP, transurethral resection of the prostate.

Appendix 3: Literature Search Strategies

Clinical Evidence Search

Search date: November 7, 2019

Databases searched: Ovid MEDLINE, Embase, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, CRD Health Technology Assessment Database, and NHS Economic Evaluation Database

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <October 2019>, EBM Reviews - Cochrane Database of Systematic Reviews <2005 to November 6, 2019>, EBM Reviews - Health Technology Assessment <4th Quarter 2016>, EBM Reviews - NHS Economic Evaluation Database <1st Quarter 2016>, Embase <1980 to 2019 Week 44>, Ovid MEDLINE(R) ALL <1946 to November 05, 2019>

Search Strategy:

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1 Prostatic Hyperplasia/ (42165)
2 ((prostat* adj2 (hyperplas* or hypertroph* or enlarg* or obstruct*)) or BPH or BPE or BPO).ti,ab,kf. (62700)
3 Lower Urinary Tract Symptoms/ (8895)
4 ((urinar* adj2 tract* adj2 symptom*) or LUTS).ti,ab,kf. (28839)
5 or/1-4 (94945)
6 Embolization, Therapeutic/ (40031)
7 (embolization* or embolisation* or embolotherap* or PAE).ti,ab,kf. (120657)
8 Polyvinyl Alcohol/ (16579)
9 (emboli* particle* or emboli* agent* or embospher* or embozen* or microspher* or PVA or polyvinyl alcohol* or (trisacryl adj2 gelatin*) or ekobi* or occlusin*).ti,ab,kf. (89940)
10 or/6-9 (218527)
11 5 and 10 (1024)
12 prostat* arter* emboli#ation.ti. (763)
13 or/11-12 (1134)
14 exp Animals/ not Humans/ (16546280)
15 13 not 14 (670)
16 Case Reports/ or Comment.pt. or Editorial.pt. or (Letter not (Letter and Randomized Controlled Trial)).pt. or Congress.pt. (5361388)
17 15 not 16 (565)
18 limit 17 to english language [Limit not valid in CDSR; records were retained] (518)
19 18 use medall,cctr,coch,clhta,cleed (277)
20 prostate hypertrophy/ (33823)
21 ((prostat* adj2 (hyperplas* or hypertroph* or enlarg* or obstruct*)) or BPH or BPE or BPO).tw,kw. (63277)
22 lower urinary tract symptom/ (17064)
23 ((urinar* adj2 tract* adj2 symptom*) or LUTS).tw,kw. (29442)
24 or/20-23 (94130)
25 arterial embolization/ (3381)
26 artificial embolization/ (8946)
27 (embolization* or embolisation* or embolotherap* or PAE).tw,kw,dv. (123371)
28 polyvinyl alcohol/ (16579)

29 (emboli* particle* or emboli* agent* or embospher* or embozen* or microspher* or PVA or polyvinyl alcohol* or (trisacryl adj2 gelatin*) or ekobi* or occlusin*).tw,kw,dv. (91006)
30 or/25-29 (213208)
31 24 and 30 (1051)
32 prostat* arter* emboli#ation.ti. (763)
33 or/31-32 (1170)
34 (exp animal/ or nonhuman/) not exp human/ (10469735)
35 33 not 34 (1128)
36 Case Report/ or Comment/ or Editorial/ or (letter.pt. not (letter.pt. and randomized controlled trial/)) or conference abstract.pt. (10845121)
37 35 not 36 (639)
38 limit 37 to english language [Limit not valid in CDSR; records were retained] (574)
39 38 use emez (293)
40 or/19,39 (570)
41 40 use medall (231)
42 40 use emez (293)
43 40 use cctr (45)
44 40 use coch (1)
45 40 use clhta (0)
46 40 use cleed (0)
47 remove duplicates from 40 (335)

Economic Evidence Search

Search date: November 22, 2019

Databases searched: Ovid MEDLINE, Embase, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Centre for Reviews and Dissemination (CRD) Health Technology Assessment Database, and National Health Service (NHS) Economic Evaluation Database

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <October 2019>, EBM Reviews - Cochrane Database of Systematic Reviews <2005 to November 20, 2019>, EBM Reviews - Health Technology Assessment <4th Quarter 2016>, EBM Reviews - NHS Economic Evaluation Database <1st Quarter 2016>, Embase <1980 to 2019 Week 46>, Ovid MEDLINE(R) ALL <1946 to November 21, 2019>

Search Strategy:

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1 Prostatic Hyperplasia/ (42296)
2 ((prostat* adj2 (hyperplas* or hypertroph* or enlarg* or obstruct*)) or BPH or BPE or BPO).ti,ab,kf. (62907)
3 Lower Urinary Tract Symptoms/ (9000)
4 ((urinar* adj2 tract* adj2 symptom*) or LUTS).ti,ab,kf. (28981)
5 or/1-4 (95278)
6 Embolization, Therapeutic/ (40165)
7 (embolization* or embolisation* or embolotherap* or PAE).ti,ab,kf. (121023)
8 Polyvinyl Alcohol/ (16630)
9 (emboli* particle* or emboli* agent* or embospher* or embozen* or microspher* or PVA or polyvinyl alcohol* or (trisacryl adj2 gelatin*) or ekobi* or occlusin*).ti,ab,kf. (90219)

10 or/6-9 (219198)
11 5 and 10 (1037)
12 prostat* arter* emboli#ation.ti. (773)
13 or/11-12 (1147)
14 economics/ (255086)
15 economics, medical/ or economics, pharmaceutical/ or exp economics, hospital/ or economics, nursing/ or economics, dental/ (843710)
16 economics.fs. (426801)
17 (econom* or price or prices or pricing or priced or discount* or expenditure* or budget* or pharmacoeconomic* or pharmaco-economic*).ti,ab,kf. (911300)
18 exp "costs and cost analysis"/ (587899)
19 (cost or costs or costing or costly).ti. (269989)
20 cost effective*.ti,ab,kf. (335430)
21 (cost* adj2 (util* or efficacy* or benefit* or minimi* or analy* or saving* or estimate* or allocation or control or sharing or instrument* or technolog*)).ab,kf. (220587)
22 models, economic/ (13048)
23 markov chains/ or monte carlo method/ (82706)
24 (decision adj1 (tree* or analy* or model*)).ti,ab,kf. (43699)
25 (markov or markow or monte carlo).ti,ab,kf. (132373)
26 quality-adjusted life years/ (41045)
27 (QOLY or QOLYs or HRQOL or HRQOLs or QALY or QALYs or QALE or QALEs).ti,ab,kf. (76678)
28 ((adjusted adj1 (quality or life)) or (willing* adj2 pay) or sensitivity analys*s).ti,ab,kf. (125099)
29 or/14-28 (2602195)
30 13 and 29 (27)
31 30 use medall,cctr,coch,clhta (7)
32 13 use cleed (0)
33 or/31-32 (7)
34 exp Animals/ not Humans/ (16536733)
35 33 not 34 (7)
36 limit 35 to english language [Limit not valid in CDSR; records were retained] (7)
37 prostate hypertrophy/ (33937)
38 ((prostat* adj2 (hyperplas* or hypertroph* or enlarg* or obstruct*)) or BPH or BPE or BPO).tw,kw. (63483)
39 lower urinary tract symptom/ (17169)
40 ((urinar* adj2 tract* adj2 symptom*) or LUTS).tw,kw. (29584)
41 or/37-40 (94458)
42 arterial embolization/ (3420)
43 artificial embolization/ (9042)
44 (embolization* or embolisation* or embolotherap* or PAE).tw,kw,dv. (123739)
45 polyvinyl alcohol/ (16630)
46 (emboli* particle* or emboli* agent* or embospher* or embozen* or microspher* or PVA or polyvinyl alcohol* or (trisacryl adj2 gelatin*) or ekobi* or occlusin*).tw,kw,dv. (91285)
47 or/42-46 (213874)
48 41 and 47 (1063)
49 prostat* arter* emboli#ation.ti. (773)
50 or/48-49 (1182)
51 Economics/ (255086)
52 Health Economics/ or Pharmacoeconomics/ or Drug Cost/ or Drug Formulary/ (130062)

53 Economic Aspect/ or exp Economic Evaluation/ (460073)
54 (econom* or price or prices or pricing or priced or discount* or expenditure* or budget* or pharmacoeconomic* or pharmaco-economic*).tw,kw. (937315)
55 exp "Cost"/ (587899)
56 (cost or costs or costing or costly).ti. (269989)
57 cost effective*.tw,kw. (347913)
58 (cost* adj2 (util* or efficac* or benefit* or minimi* or analy* or saving* or estimate* or allocation or control or sharing or instrument* or technolog*)).ab,kw. (232088)
59 Monte Carlo Method/ (65684)
60 (decision adj1 (tree* or analy* or model*)).tw,kw. (47531)
61 (markov or markow or monte carlo).tw,kw. (137433)
62 Quality-Adjusted Life Years/ (41045)
63 (QOLY or QOLYs or HRQOL or HRQOLs or QALY or QALYs or QALE or QALEs).tw,kw. (80553)
64 ((adjusted adj1 (quality or life)) or (willing* adj2 pay) or sensitivity analys*s).tw,kw. (145982)
65 or/51-64 (2232084)
66 50 and 65 (38)
67 (exp animal/ or nonhuman/) not exp human/ (10486212)
68 66 not 67 (38)
69 limit 68 to english language [Limit not valid in CDSR; records were retained] (38)
70 69 use emez (22)
71 36 or 70 (29)
72 71 use medall (6)
73 71 use emez (22)
74 71 use cctr (1)
75 71 use coch (0)
76 71 use clhta (0)
77 71 use cleed (0)
78 remove duplicates from 71 (23)

Grey Literature Search

Performed: November 25–27, 2019; updated August 14, 2020

Websites searched: HTA Database Canadian Repository, Alberta Health Evidence Reviews, BC Health Technology Assessments, Canadian Agency for Drugs and Technologies in Health (CADTH), Institut national d'excellence en santé et en services sociaux (INESSS), Institute of Health Economics (IHE), McGill University Health Centre Health Technology Assessment Unit, Centre Hospitalier de l'Universite de Quebec-Universite Laval, Health Technology Assessment Database, Epistemonikos, National Institute for Health and Care Excellence (NICE), Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Centers, Australian Government Medical Services Advisory Committee, Council of Australian Governments Health Technologies, Centers for Medicare & Medicaid Services Technology Assessments, Institute for Clinical and Economic Review, Ireland Health Information and Quality Authority Health Technology Assessments, Washington State Health Care Authority Health Technology Reviews, Health Technology Wales, Oregon Health Authority Health Evidence Review Commission, Veterans Affairs Health Services Research and Development, Italian National Agency for Regional Health Services (AGENAS), Australian Safety and Efficacy Register of New Interventional Procedures -Surgical (ASERNIP-S), Belgian Health Care Knowledge Centre, Ludwig Boltzmann Institute for Health Technology Assessment, Ministry of Health Malaysia Health Technology Assessment Section, Swedish Agency for Health Technology Assessment and Assessment of Social Services, PROSPERO, EUnetHTA, Tuft's Cost-Effectiveness Analysis Registry

Keywords used:
prostate, prostatic, embolization, embolisation, prostate artery embolization, prostate artery embolisation, prostatic artery embolization, prostatic artery embolisation, prostate arterial embolization, prostate arterial embolisation, PAE, benign prostatic hyperplasia

Clinical results (included in PRISMA): 6
Economic results (included in PRISMA): 6
Ongoing clinical trials: 28
Ongoing HTAs (PROSPERO/EUnetHTA): 4

Appendix 4: Critical Appraisal of Clinical Evidence

Table A3: Risk of Bias[a] Among Randomized Controlled Trials (Cochrane Risk of Bias Tool)

Author, Year	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Incomplete Outcome Data	Selective Reporting	Other Bias
Prostatic Artery Embolization Versus Transurethral Resection of the Prostate						
Abt et al, 2018[14]	Low	Low	Low[b]	Low	Low	High[c]
Carnevale et al, 2016[39]	Unclear	Unclear	Unclear	Low	Low	High[d,e]
Gao et al, 2014[13]	Low	High[f]	Low[b]	Low	High[g]	High[h]
Insausti et al, 2020[16]	Low	Unclear	Low[b]	Low	Low	High[e]

[a]Possible risk of bias levels: Low, High, and Unclear.
[b]No blinding occurred, but due to the differences in the nature of the two procedures, blinding would not have been possible.
[c]Only interim 12-week results of a 2-year study are available.
[d]Peak urinary flow rate and bladder contractility index scores were significantly different between groups at baseline.
[e]Number of study participants too small to achieve adequate power.
[f]Patients were made aware of their allocation before the procedure and could choose to undergo the procedure or not. Only patients who agreed to their allocation were included in the analysis.
[g]Unclear definition of "early" and "late" outcomes.
[h]Some patients had repeat procedures.

Table A4: Risk of Bias[a] Among Nonrandomized Trials (ROBINS-I Tool)

	Pre-Intervention		At Intervention		Post-Intervention		
Author, Year	Confounding	Study Participation Selection	Classification of Interventions	Deviations From Intended Intervention	Missing Data	Measurement of Outcomes	Selection of Reported Results
Prostatic Artery Embolization Versus Transurethral Resection of the Prostate							
Ray et al, 2018[15]	Low	Moderate[b]	Low	Low	Moderate[c]	Moderate[d]	Moderate[e]
Prostatic Artery Embolization Versus Open Simple Prostatectomy							
Russo et al, 2015[17]	Moderate[f]	Moderate[f]	Low	Low	Low	Low	Low

Abbreviation: ROBINS-I, Risk of Bias in Non-randomized Studies—of Interventions.
[a]Possible risk of bias levels: Low, Moderate, Serious, Critical, and No Information.
[b]Study authors note difficulty in recruiting participants for the transurethral resection of the prostate (TURP) group (79 participants in the TURP group compared with 206 for prostatic artery embolization [PAE] at baseline).
[c]Higher percentage of participants in the PAE group than the TURP group responded to follow-up questionnaires (74% vs. 48%, respectively).
[d]Complications were patient-reported using follow-up questionnaires.
[e]Unclear timing of patient-reported outcomes.
[f]1:1 matched-pair analysis using prostate volume, peak flow, post-void residual volume, and International Prostate Symptom Score.

Table A5: GRADE Evidence Profile for Comparison of Prostatic Artery Embolization Versus Transurethral Resection of the Prostate

Number of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
International Prostate Symptom Score at 3 Months							
4 (3 RCTs, 1 observational)	Serious limitations (−1)	Serious limitations (−1)	No serious limitations	Serious limitations (−1)	Undetected	None	⨁ Very low
International Prostate Symptom Score at 6 Months							
3 (2 RCTs, 1 observational)	Serious limitations (−1)	Serious limitations (−1)	No serious limitations	Serious limitations (−1)	Undetected	None	⨁ Very low
International Prostate Symptom Score at 12 Months							
4 (3 RCTs, 1 observational)	Serious limitations (−1)	Serious limitations (−1)	No serious limitations	Serious limitations (−1)	Undetected	None	⨁ Very low
International Prostate Symptom Score at 24 Months							
1 (RCT)	Serious limitations (−1)	No serious limitations	No serious limitations	Serious limitations (−1)	Undetected	None	⨁⨁ Low
Health-Related Quality of Life at 3 Months							
4 (3 RCTs, 1 observational)	Serious limitations (−1)	Serious limitations (−1)	No serious limitations	Serious limitations (−1)	Undetected	None	⨁ Very low
Health-Related Quality of Life at 6 Months							
3 (2 RCTs, 1 observational)	Serious limitations (−1)	No serious limitations	No serious limitations	Serious limitations (−1)	Undetected	None	⨁⨁ Low
Health-Related Quality of Life at 12 Months							
4 (3 RCTs, 1 observational)	Serious limitations (−1)	Serious limitations (−1)	No serious limitations	Serious limitations (−1)	Undetected	None	⨁ Very low
Health-Related Quality of Life at 24 Months							
1 (RCT)	Serious limitations (−1)	No serious limitations	No serious limitations	Serious limitations (−1)	Undetected	None	⨁⨁ Low
Erectile Function at 3 Months							
2 (1 RCT, 1 observational)	Serious limitations (−1)	Serious limitations (−1)	No serious limitations	Serious limitations (−1)	Undetected	None	⨁ Very low

Number of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Erectile Function at 6 Months							
1 (observational)	Serious limitations (−1)	No serious limitations	No serious limitations	Serious limitations (−1)	Undetected	None	⊕ Very low
Erectile Function at 12 Months							
2 (1 RCT, 1 observational)	Serious limitations (−1)	Serious limitations (−1)	No serious limitations	Serious limitations (−1)	Undetected	None	⊕ Very low
4 (3 RCTs, 1 observational)	Serious limitations (−1)	No serious limitations	No serious limitations	Serious limitations (−1)	Undetected	None	⊕⊕ Low
Peak Urinary Flow Rate at 3 Months							
4 (3 RCTs, 1 observational)	Serious limitations (−1)	No serious limitations	No serious limitations	Serious limitations (−1)	Undetected	None	⊕⊕ Low
Peak Urinary Flow Rate at 6 Months							
3 (2 RCTs, 1 observational)	Serious limitations (−1)	No serious limitations	No serious limitations	Serious limitations (−1)	Undetected	None	⊕⊕ Low
Peak Urinary Flow Rate at 12 Months							
4 (3 RCTs, 1 observational)	Serious limitations (−1)	No serious limitations	No serious limitations	Serious limitations (−1)	Undetected	None	⊕⊕ Low
Peak Urinary Flow Rate at 24 Months							
1 (RCT)	Serious limitations (−1)	No serious limitations	No serious limitations	Serious limitations (−1)	Undetected	None	⊕⊕ Low
Post-Void Residual Volume at 3 Months							
4 (3 RCTs, 1 observational)	Serious limitations (−1)	Serious limitations (−1)	No serious limitations	Serious limitations (−1)	Undetected	None	⊕ Very low
Post-Void Residual Volume at 6 Months							
3 (2 RCTs, 1 observational)	Serious limitations (−1)	No serious limitations	No serious limitations	Serious limitations (−1)	Undetected	None	⊕⊕ Low
Post-Void Residual Volume at 12 Months							
4 (3 RCTs, 1 observational)	Serious limitations (−1)	Serious limitations (−1)	No serious limitations	Serious limitations (−1)	Undetected	None	⊕ Very low

Number of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Post-Void Residual Volume at 24 Months							
1 (RCT)	Serious limitations (−1)	No serious limitations	No serious limitations	Serious limitations (−1)	Undetected	None	⨁⨁ Low
Prostate Volume at 3 Months							
4 (3 RCTs, 1 observational)	Serious limitations (−1)	No serious limitations	No serious limitations	Serious limitations (−1)	Undetected	None	⨁⨁ Low
Prostate Volume at 6 Months							
3 (2 RCTs, 1 observational)	Serious limitations (−1)	No serious limitations	No serious limitations	Serious limitations (−1)	Undetected	None	⨁⨁ Low
Prostate Volume at 12 Months							
4 (3 RCTs, 1 observational)	Serious limitations (−1)	No serious limitations	No serious limitations	Serious limitations (−1)	Undetected	None	⨁⨁ Low
Prostate Volume at 24 Months							
1 (RCT)	Serious limitations (−1)	No serious limitations	No serious limitations	Serious limitations (−1)	Undetected	None	⨁⨁ Low
Prostate-Specific Antigen Level at 3 Months							
3 (RCTs)	Serious limitations (−1)	Serious limitations (−1)	Serious limitations (−1)	Serious limitations (−1)	Undetected	None	⨁ Very low
Prostate-Specific Antigen Level at 6 Months							
2 (RCTs)	Serious limitations (−1)	No serious limitations	Serious limitations (−1)	Serious limitations (−1)	Undetected	None	⨁ Very low
Prostate-Specific Antigen Level at 12 Months							
3 (RCTs)	Serious limitations (−1)	No serious limitations	Serious limitations (−1)	Serious limitations (−1)	Undetected	None	⨁ Very low
Prostate-Specific Antigen Level at 24 Months							
1 (RCT)	Serious limitations (−1)	No serious limitations	Serious limitations (−1)	Serious limitations (−1)	Undetected	None	⨁ Very low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation; RCT, randomized controlled trial.

Table A6: GRADE Evidence Profile for Comparison of Prostatic Artery Embolization Versus Open Prostatectomy

Number of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
International Prostate Symptom Score at 6 and 12 Months							
1 (observational)	Serious limitations (−1)	No serious limitations	No serious limitations	Serious limitations (−1)	Undetected	None	⊕ Very low
Health-Related Quality of Life at 12 Months							
1 (observational)	Serious limitations (−1)	No serious limitations	No serious limitations	Serious limitations (−1)	Undetected	None	⊕ Very low
Erectile Function at 6 and 12 Months							
1 (observational)	Serious limitations (−1)	No serious limitations	No serious limitations	Serious limitations (−1)	Undetected	None	⊕ Very low
Peak Urinary Flow Rate at 6 and 12 Months							
1 (observational)	Serious limitations (−1)	No serious limitations	No serious limitations	Serious limitations (−1)	Undetected	None	⊕ Very low
Post-Void Residual Volume at 6 and 12 Months							
1 (observational)	Serious limitations (−1)	No serious limitations	No serious limitations	Serious limitations (−1)	Undetected	None	⊕ Very low
Prostate-Specific Antigen Level at 6 and 12 Months							
1 (observational)	Serious limitations (−1)	No serious limitations	Serious limitations (−1)	Serious limitations (−1)	Undetected	None	⊕ Very low

Abbreviation: GRADE, Grading of Recommendations Assessment, Development, and Evaluation

Appendix 5: Selected Excluded Studies—Economic Evidence

For transparency, we provide a list of studies that readers might have expected to see but that did not meet the inclusion criteria, along with the primary reason for exclusion.

Table A7: Excluded Studies

Citation	Primary Reason for Exclusion
Bagla S, Smirniotopoulos J, Orlando J, Piechowiak R. Cost analysis of prostate artery embolization (PAE) and transurethral resection of the prostate (TURP) in the treatment of benign prostatic hyperplasia. Cardiovasc Intervent Radiol. 2017;40(11):1694-7.	Costing only
Bagla S, Smirniotopoulos J, Orlando JC, Piechowiak R. Robotic-assisted versus manual prostatic arterial embolization for benign prostatic hyperplasia: a comparative analysis. Cardiovasc Intervent Radiol. 2017;40(3):360-5.	Compared types of PAE, not with other BPH alternatives
Brown AD, Stella SF, Simons ME. Minimally invasive treatment for benign prostatic hyperplasia: economic evaluation from a standardized hospital case costing system. Cardiovasc Intervent Radiol. 2019;42(4):520-7.	Costing only
Mullhaupt G, Hechelhammer L, Engeler DS, Gusewell S, Betschart P, Zumstein V, et al. In-hospital cost analysis of prostatic artery embolization compared with transurethral resection of the prostate: post hoc analysis of a randomized controlled trial. BJU Int. 2019;123(6):1055-60.	Costing only
Okun J, Siddiqi M, Shukla P. Abstract No. 450 Cost analysis of prostate artery embolization and medical management in the treatment of benign prostatic hyperplasia. J Vasc Int Radiol. 2019;30(3 Supplement):S196-S7.	Costing and abstract only
Rajaratnam D, Yagnik V, Shi V, Smith J. Comparative cost analysis of prostate artery embolization to modern surgical techniques in the treatment of symptomatic large volume benign prostatic hyperplasia. J Vasc Int Radiol. 2016;27(3):S55-S6.	Costing and abstract only
Roebker J, Chadalavada S. Abstract No. 122 Economics of embolization: the competitive advantage of prostatic artery embolization in value-based care. J Vasc Int Radiol. 2019;30(3 Supplement):S57.	Abstract only

Appendix 6: Economic Evidence—Summary of Costing Studies and Abstracts

Table A8: Summary of Costing Studies

Author, Year, Country	Perspective	Population	Intervention and Comparator	Results
Bagla et al, 2017,[51] United States	US hospital perspective	Adults with LUTS from BPH (N = 156)	• PAE • TURP	2014 USD Procedural costs: • PAE: $1,667 • TURP: $2,154 Total in-hospital costs: • PAE: $1,678 • TURP: $5,338
Brown et al, 2019,[31] Canada	Ontario hospital perspective	Adults with LUTS from BPH (N = 266)	• PAE • TURP • PVP	2017 USD • PAE: $3,868 • TURP: $4,101 • PVP: $4,622
Mullhaupt et al, 2019,[52] Switzerland	Swiss hospital perspective	Adults with LUTS from BPH (N = 99)	• PAE • TURP	2017 EUR • PAE: €8,185 • TURP: €9,137
Okun et al, 2019,[118] United States (abstract only)	US hospital / Medicare perspective	Adults (aged 51–60) with LUTS from BPH	• PAE • Medications	2019 USD • PAE: $1,678 • Medication: $138 per month • PAE cost equivalent to 12.2 months of medication
Rajaratnam et al, 2016,[87] United States (abstract only)	US hospital perspective	Adults with LUTS from BPH	• PAE • HoLEP • Open prostatectomy	2016 USD • PAE: $3,342 • HoLEP: $8,380 • Open prostatectomy: $5,862
Roebker et al, 2019,[119] United States (abstract only)	US hospital perspective	Adults with LUTS from BPH	• PAE • TURP • Convective radiofrequency • Conductive radiofrequency • UroLift • HoLEP • PVP	2019 USD Cost per unit decrease in IPSS: • PAE: $119 • TURP: $309 • RF (Rezum): $222 • Conductive RF (Protista): $254 • UroLift: $600 • HoLEP: $195 • PVP: $338 ICER (PAE as reference): • TURP: $1,473 • RF, conductive RF, UroLift: dominated (more costly, less effective) • HoLEP: $403 • PVP: $5,279

Abbreviations: BPH, benign prostatic hyperplasia; HoLEP, holmium laser enucleation of the prostate; IPSS, International Prostate Symptom Score; LUTS, lower urinary tract symptoms; PAE, prostatic artery embolization; PVP, photoselective vaporization of the prostate; RF, convective radiofrequency; TURP, transurethral resection of the prostate.

Appendix 7: Primary Economic Evaluation

Alternative Primary Study Comparing PAE to TURP (Carnevale et al)[39]

While this scenario has the same comparison as the reference case (PAE versus TURP), we used an alternative primary study by Carnevale et al[39] as the source of baseline characteristics, IPSS change, and technical and clinical failures. Compared to the study used in our reference case,[13] IPSS reduction from baseline[39] was similar for PAE but greater for TURP.[39] We changed a number of clinical parameters for this scenario, including the starting age, baseline IPSS, IPSS reduction due to treatment, and the probability of technical and clinical failure. Table A5 lists the parameters used in this scenario that are different from the reference case. Other adverse event data were not changed due to the limited information on adverse events in the study. The authors provided IPSS reduction from baseline at 12 months. We adjusted the 12-month IPSS reduction to match the cycle length (i.e., 3 months) used in our model.

Carnevale et al[39] had different definitions of technical and clinical failure than what we used in the reference case analysis. In the reference case, technical failure was defined as the failure to achieve embolization on at least one side of the pelvis (unilateral embolization), whereas Carnevale et al[63] specified this as the failure to achieve both sides of the pelvis (bilateral embolization). The IPSS component of the clinical failure criteria used by Carnevale and colleagues was an overall IPSS of ≥ 8, whereas in the reference case the IPSS criteria included IPSS improvement of ≤ 25% as well as the overall IPSS (i.e., IPSS ≥ 18 or ≥ 15, depending on the source).[13,68] As the criteria by Carnevale et al[63] is much broader, we also applied an additional failure criteria (i.e., IPSS reduction of ≤ 25% of baseline) in our model to ensure we selected those with unsatisfactory IPSS to experience clinical failure first.

Table A9: Parameters Used in the Economic Model—Alternative Primary Study (Carnevale et al[39]) Comparing PAE to TURP

Parameter	Scenario	Reference Case
Baseline Characteristics		
Starting age (years)	64.95[a]	67.05
Starting IPSS	26.45[a]	22.95
IPSS Change[b]		
PAE	0–12 mo: −12.50 (95% CI: −29.69, 4.69)[a]	0–3 mo: −8.70 (95% CI: −18.55, 1.15) 3–6 mo: −2.80 (95% CI: −12.34, 6.74) 6–12 mo: −1.90 (95% CI: −9.08, 5.28) 12–24 mo: −2.20 (95% CI: −8.00, 3.60) Total reduction over 2 y: −15.60
TURP	0–12 mo: −21.50 (95% CI: −39.49, −3.51)[a]	0–3 mo: −13.70 (95% CI: −21.41, −5.99) 3–6 mo: 0.30 (95% CI: −6.42, 7.02)

Parameter	Scenario	Reference Case
		6–12 mo: −1.10 (95% CI: −7.66, 5.46) 12–24 mo: −1.80 (95% CI: −7.82, 4.22) Total reduction over 2 y: −16.30
Technical and Clinical Failure		
PAE technical failure[c]	13.33%[a]	5.26%
PAE clinical failure[d]		
End of year 1 or 2	Year 1: 13.33%[a,e]	Year 2: 9.26%[f]
Each subsequent year (to the end of time horizon: 6.5 y)	6.07%[g]	3.86%[g]
TURP clinical failure[d]		
End of year 1 or 2	Year 1: 0%[a,e]	Year 2: 3.77%[f]
Each subsequent year (to the end of time horizon: 6.5 y)	3.63%[g,h]	2.90%[g]

Abbreviations: IPSS, International Prostate Symptom Score; PAE, prostatic artery embolization; TURP, transurethral resection of the prostate.

[a]Obtained from Carnevale et al, 2016.[63]

[b]IPSS change was applied as IPSS change per 3-month cycle. The 95% confidence interval was calculated using standard deviation to reflect individual-level variability, which was required in the microsimulation model. The 95% confidence interval in this table may differ from the 95% confidence interval reported in the Clinical Evidence Review, above. We used standard error in the Clinical Evidence Review to calculate the 95% confidence interval, which took into consideration the sample size of the study to reflect cohort-level variability instead of individual-level variability.

[c]In this scenario, the definition of technical failure is failure to achieve bilateral embolization (i.e., embolization on both left and right sides). In the reference case, the definition is failure to achieve unilateral embolization (i.e., embolization on either the left or right side).

[d]We calibrated our model parameters against these probabilities to ensure the rate of clinical failure in our model matched that found by Carnevale et al, 2016.[39]

[e]IPSS criteria for clinical failure: IPSS ≥ 8. Criteria is based on Carnevale et al, 2016.[63] In this model, those meeting the criteria and experience a decrease in IPSS of ≤ 25% would fail first, followed by those with meeting one of the two components (if any).

[f]IPSS criteria for clinical failure: decrease in IPSS of ≤ 25% and/or IPSS ≥ 18. Criteria is based on Gao et al, 2014.[13] In this model, those meeting both criteria would fail first, followed by those meeting one of the two components (if any).

[g]IPSS criteria for clinical failure: decrease in IPSS of ≤ 25% and/or IPSS ≥ 15. Criteria is based on Pisco et al, 2016.[68] In this model, those meeting both criteria would fail first, followed by those meeting one of the two components (if any).

[h]Source: Strope et al, 2015.[74] IPSS criteria not reported. We applied the same criteria as in the reference case.

Notes on Clinical Failure and Model Calibration

The goal of calibration was to match our model output on the proportion of clinical failure to the proportion reported in the literature. Using TreeAge Pro,[75] we created payoffs that calculate the proportion of the cohort experiencing clinical failure at two time points: at the end of 2 years and at end of the time horizon. We also created new variables that represent percentages, which were calibrated and applied to those meeting the IPSS failure thresholds, to estimate the proportion of clinical failure. The calibration process adjusts the value of the percentages iteratively until the resulting model output match the literature data. The calibrated percentages are presented in Table A6. Note, the calibrated percentages at the end of year 2 were applied once in the model, whereas the percentages from the start of year 3 to the end of time horizon were applied in every cycle (i.e., every 3 months). The latter is

applied every cycle because IPSS failure is assessed every cycle; the calibrated percentage is subsequently applied to the people who met one or both of the IPSS failure thresholds—a decrease in IPSS of ≤ 25% from baseline and IPSS ≥ 15—during that cycle.

Using the Calibration function in TreeAge, we selected Microsimulation as the analysis type in the Setup tab. We used 15,000 trials and 100 samples when iterating the payoff results. In the Inputs tab, we selected the variables to be calibrated and set each to have a lower and upper bound of 0% and 100%. In the Targets tab, we selected the payoffs representing the model output of clinical failure and we specified the target value to be the reported values from primary studies. Each PAE and TURP strategy had equal weighting during calibration. We ran calibration until the process stopped (i.e., when the generated Goodness of Fit value was as close to 0 as possible).

Table A10: Calibrated Parameters Used in the Economic Model

	Percentage Experiencing Clinical Failure
Reference Case	
End of Year 2 (1-time percentage)	
PAE	
Met both IPSS failure criteria	100%
Met one IPSS failure criterion	14.89%
TURP	
Met both IPSS failure criteria	76.80%
Met one IPSS failure criterion	0%
Start of Year 3 to end of time horizon (% per cycle)	
PAE	
Met both IPSS failure criteria	100%
Met one IPSS failure criterion	1.64%
TURP	
Met both IPSS failure criteria	100%
Met one IPSS failure criterion	0.546%
Scenario 1: Alternative Primary Study (PAE vs. TURP): Carnevale et al, 2016[63]	
End of Year 1 (1-time percentage)	
PAE	
Met both IPSS failure criteria	60.50%
Met one IPSS failure criterion	0%
TURP	
Met both IPSS failure criteria	0%
Met one IPSS failure criterion	0%
Start of Year 2 to end of time horizon (% per cycle)	
PAE	
Met both IPSS failure criteria	6.60%

	Percentage Experiencing Clinical Failure
Met one IPSS failure criterion	0%
TURP	
Met both IPSS failure criteria	5.42%
Met one IPSS failure criterion	0%
Scenario 3: PAE vs. OSP	
End of Year 1 (1-time percentage)	
PAE	
Met both IPSS failure criteria	18.16%
Met one IPSS failure criterion	0%
OSP	
Met both IPSS failure criteria	53.97%
Met one IPSS failure criterion	0%
Start of Year 2 to end of time horizon (% per cycle)	
PAE	
Met both IPSS failure criteria	4.83%
Met one IPSS failure criterion	0%
OSP	
Met both IPSS failure criteria	69.80%
Met one IPSS failure criterion	0%
Scenario 4: Shorter Treatment Effect for PAE	
End of Year 2 (1-time percentage)	
PAE	
Met both IPSS failure criteria	Unchanged from reference case
Met one IPSS failure criterion	Unchanged from reference case
TURP	
Met both IPSS failure criteria	Unchanged from reference case
Met one IPSS failure criterion	Unchanged from reference case
Start of Year 3 to end of time horizon (% per cycle)	
PAE	
Met both IPSS failure criteria	7.25%
Met one IPSS failure criterion	0%
TURP	
Met both IPSS failure criteria	Unchanged from reference case
Met one IPSS failure criterion	Unchanged from reference case

Abbreviations: IPSS, International Prostate Symptom Score; OSP, open simple prostatectomy; PAE, prostatic artery embolization; TURP, transurethral resection of the prostate.

Open Simple Prostatectomy Scenario

This scenario compared PAE with OSP (instead of TURP, as in the reference case). Several parameters were modified, including the starting age, baseline IPSS, IPSS reduction due to treatment, adverse events, cost of the procedure, and time horizon. Most clinical inputs were obtained from the only relevant comparative study identified in our clinical review (Russo et al[65]). Since this study had only 1 year of follow-up, we obtained a longer-term clinical failure rate for OSP from the literature.[120] The costs of OSP were obtained from the Schedule of Benefits for physician fees and the Ontario Case Costing tool for hospital costs.[83,121] Table A7 lists the parameters used in this scenario that are different from the reference case.

Table A11: Parameters Used in the Economic Model—Open Simple Prostatectomy Scenario

Parameter	Scenario	Reference Case
Baseline Characteristics		
Starting age (years)	67.69[a]	67.05
Starting IPSS	23.67[a]	22.95
IPSS Change[b]		
PAE	0–6 mo: −12.63 (95% CI: −25.74, 0.48)[a] 6–12 mo: −0.95 (95% CI: −11.91, 10.01)[a] Total reduction over 1 y: −13.58[a]	0–3 mo: −8.70 (95% CI: −18.55, 1.15) 3–6 mo: −2.80 (95% CI: −12.34, 6.74) 6–12 mo: −1.90 (95% CI: −9.08, 5.28) 12–24 mo: −2.20 (95% CI: −8.00, 3.60) Total reduction over 2 yr:−15.60
Comparator	0–6 mo: −18.42 (95% CI: −29.65, −7.19)[a] 6–12 mo: −0.62 (95% CI: −9.43, 8.19)[a] Total reduction over 1 y: −19.04[a]	0–3 mo: −13.70 (95% CI: −21.41, −5.99) 3–6 mo: 0.30 (95% CI: −6.42, 7.02) 6–12 mo: −1.10 (95% CI: −7.66, 5.46) 12–24 mo: −1.80 (95% CI: −7.82, 4.22) Total reduction over 2 y: −16.30
Adverse Events[c]	**OSP**	**TURP**
Clinical failure		
End of year 1 or 2	Year 1: 1.80%[d]	Year 2: 3.77%[e]
Each subsequent year (to the end of time horizon: 6.5 y)	2.13%[d]	2.90%[f]

Parameter	Scenario	Reference Case
Incontinence	3.75%[a,g]	10.61%
Blood transfusion	6.25%[a,h]	3.77%
Urethral stricture or bladder neck contracture	2.50%[a,i]	4.17%
Disutility of procedure	−0.096[122]	−0.051
Costs ($)	**OSP**	**TURP**
Physician fees	867.60[j]	615.71
Hospital costs	7,763.00[k]	5,556.79

Abbreviations: IPSS, International Prostate Symptom Score; OSP, open simple prostatectomy; PAE, prostatic artery embolization; TURP, transurethral resection of the prostate.

[a]Obtained from the only relevant comparative study on PAE versus OSP (Russo et al.)[17]

[b]IPSS change was applied as IPSS change per 3-month cycle. The 95% confidence interval was calculated using standard deviation to reflect individual-level variability, which was required in the microsimulation model. The 95% confidence interval in this table may differ from the 95% confidence interval reported in the Clinical Evidence Review, above. We used standard error in the Clinical Evidence Review to calculate the 95% confidence interval, which took into consideration the sample size of the study to reflect cohort-level variability instead of individual-level variability.

[c]Other TURP adverse events are not included in OSP scenario.

[d]Obtained from Eredics et al, 2018.[120] We calibrated our model parameters against these probabilities to ensure the rate of clinical failure in our model matched. IPSS criteria was not reported, so we applied the same criteria as the reference case.

[e]IPSS criteria for clinical failure: decrease in IPSS of ≤ 25% and/or IPSS ≥ 18. Criteria is based on Gao et al, 2014.[13] In this model, those meeting both criteria would fail first, followed by those meeting one of the two components (if any).

[f]IPSS criteria for clinical failure: decrease in IPSS of ≤25% and/or IPSS ≥15. Criteria is based on Pisco et al, 2016.[68] In this model, those meeting both criteria would fail first, followed by those meeting one of the two components (if any).

[g]Probability presented here is the probability over a 1-year period (annual probability). Probability is adjusted in the model as 3-month probability to reflect the cycle length.

[h]Probability presented here is applied as a one-time probability in the model.

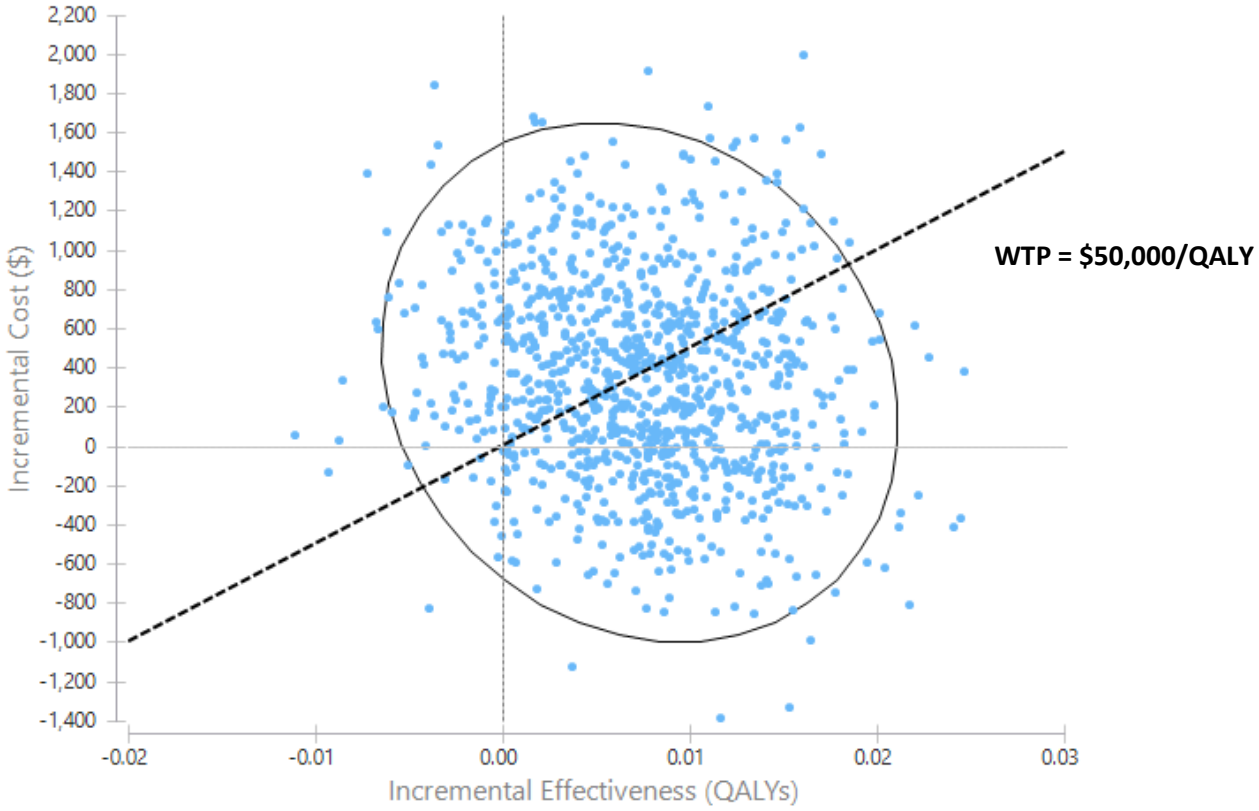
[i]Probability presented here is the probability over a 2-year period. Probability is adjusted in the model as 3-month probability to reflect the cycle length.

[j]Cost obtained from the Schedule of Benefits.[83]

[k]Cost obtained from the Ontario Case Costing tool.[121]

Cost-Effectiveness Plane

Figure A1: Scatter Plot of 1,000 Simulated Pairs of Incremental Costs and Effects in the Cost-Effectiveness Plane: PAE Versus TURP, Reference Case



Abbreviations: PAE, prostatic artery embolization; QALY, quality-adjusted life year; TURP, transurethral resection of the prostate; WTP, willingness-to-pay.
Note: costs in 2020 CAD.

Appendix 8: Letter of Information[1]

LETTER OF INFORMATION

Health Quality Ontario is conducting a review of **Prostatic Artery Embolization (PAE),** a treatment for benign prostatic hyperplasia (BPH). The purpose is to understand whether this treatment should be more broadly funded in Ontario.

An important part of this review involves speaking to patients and family members of those who may have experience with BPH and the prostatic artery embolization treatment, or who may have attempted to access it. Our goal is always to make sure the lived-experience of individuals and families are considered in the funding recommendations for this test.

WHAT DO YOU NEED FROM PARTICIPANTS?

- ✓ 20-30 minutes of time for a phone or in-person interview to hear about their experiences
- ✓ Permission to audio- (not video-) record the interview

WHAT PARTICIPATION INVOLVES

If a participant agrees to share their experiences, they will be asked to have an interview with Health Quality Ontario staff. The interview will likely last 20-30 minutes. It will be held in a private location or over the telephone. With consent, the interview will be audio-recorded. The interviewer will ask questions about perspectives of BPH, decision-making and more general thoughts about the PAE and the use of this procedure in Ontario.

Participation is voluntary. Those who volunteer may decide not to participate, refuse to answer any questions or withdraw before the interview. Withdrawal will in no way affect the care received.

CONFIDENTIALITY

All information collected for the review will be kept confidential and privacy will be protected except as required by law. The results of this review will be published, however no identifying information will be released or published. Any records containing information from the interview will be stored securely.

RISKS TO PARTICIPATION:

There are no known physical risks to participating. Some participants may experience discomfort or anxiety after speaking about their lived experience. If this is the case, participants can speak to our staff.

If you have any questions, please contact Health Quality Ontario staff:

[1] Health Quality Ontario is now part of Ontario Health.

Appendix 9: Interview Guide[2]

Interview for Prostatic Artery Embolization (PAE) HTA

Intro
Explain HQO purpose, HTA process, and purpose of interview

Lived- Experience
Development of symptoms
Impact of symptoms on quality of life
Medical journey to receiving diagnosis and subsequent therapies

Treatments for BPH
Decision-making surrounding different treatment options
Information about different treatments – readily available?
Access to treatments; any barriers that existed?

PAE
Information about PAE (if applicable)
Decision-making around undergoing PAE (if applicable)
Procedure itself and impact of PAE; quality of life, side effects, etc.

Overall thoughts on the use of PAE and its potential impact?

[2] Health Quality Ontario (HQO) is now part of Ontario Health.

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