

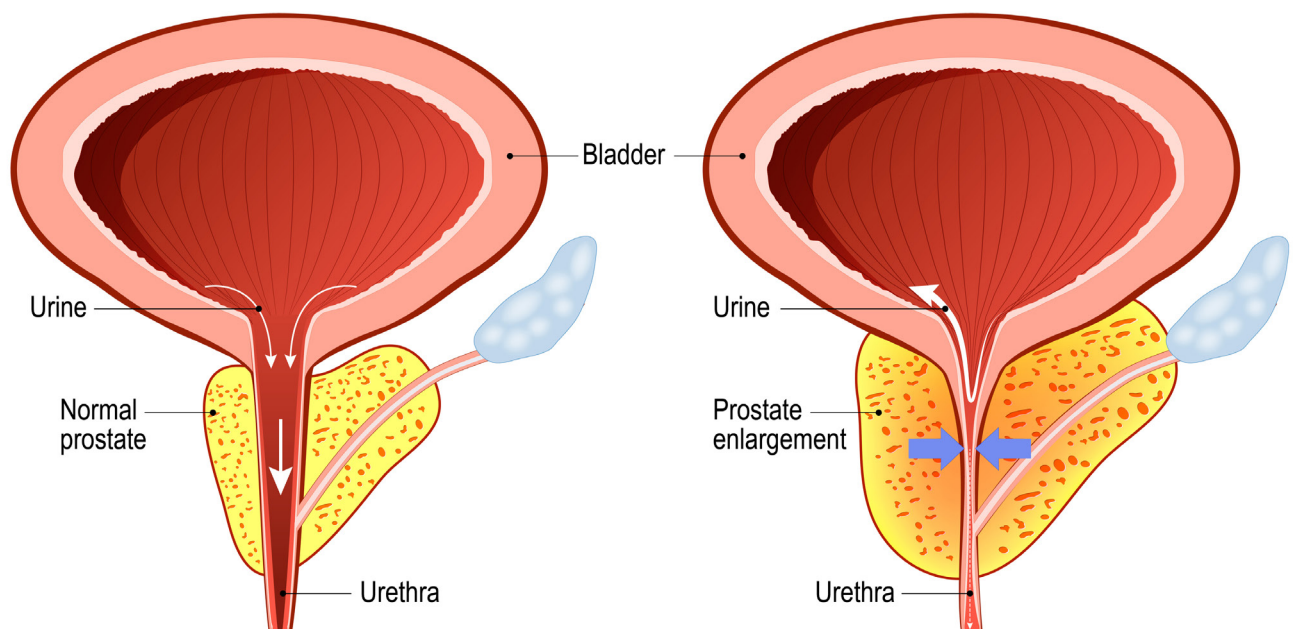
# CADTH ISSUES IN EMERGING HEALTH TECHNOLOGIES

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## Minimally Invasive Treatments for Lower Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia



iStock Image: Benign Prostatic Hyperplasia

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## Methods

CADTH Horizon Scanning bulletins present an overview of the technology and available evidence. They are not systematic reviews and do not involve critical appraisal or include a detailed summary of study findings. At this point in the development and diffusion of these technologies, critical appraisal of the available evidence may be useful for decision-makers. The evidence provided in the summary of the evidence section of this bulletin is therefore largely based on a [2019 Rapid Response Report with Critical Appraisal](#)<sup>16</sup> that was produced to support this bulletin. A detailed summary of studies included in the Rapid Response Report is available in the report.

### Literature Search Strategy

A limited literature search was conducted by an information specialist on key resources including PubMed, the Cochrane Library, the University of York Centre for Reviews and Dissemination databases, the websites of Canadian and major international health technology agencies, as well as a focused Internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and additional keywords. The main search concepts were urethral lift, water vapour thermal therapy, embolization, and aquablation, and lower urinary tract symptoms due to BPH. Search filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, or network meta-analyses, and randomized controlled trials or controlled clinical trials. Where possible, retrieval was limited to the human population. The search was limited to English language documents published between January 1, 2016 and July 29, 2019. A modified monthly update search for new studies was run in PubMed from August 2019 until January 2020.

### Study Selection

One author screened the literature search results and reviewed the full text of all potentially relevant studies. This bulletin builds on a 2019 CADTH Rapid Response Report prepared to support this bulletin<sup>16</sup> and other assessments conducted by the National Institute for Health and Care Excellence (NICE), in the UK, the ECRI Institute, in the US, and other health technology assessment agencies. Individual studies included in these earlier assessments have not been described, but more recent studies have been included if they contribute further information.

### Peer Review

A draft version of this bulletin was reviewed by two clinical experts. Manufacturers' comments were also solicited and considered.

## Summary

- This bulletin builds on a [CADTH Rapid Response Report](#) that critically appraises recent evidence on treatments to alleviate lower urinary tract symptoms caused by benign prostatic hyperplasia (BPH).
- The focus of this bulletin is on four treatments:
  - prostatic urethral lift (the UroLift system)
  - water vapour thermal therapy (the Rezūm system)
  - prostatic artery embolization (using various commercial embolizing agents)
  - aquablation (the AquaBeam system).
- Evidence to date suggests these treatments can improve lower urinary tract symptoms, but, in terms of symptom relief, they may be less effective than conventional treatments, such as transurethral resection of the prostate (TURP).
- Patients may be willing to accept less effective symptom relief as a trade off for fewer adverse events, shorter recovery time, and less risk of ejaculatory and erectile dysfunction with these less invasive treatments.
- The availability of less invasive treatment options for BPH may encourage more individuals to undergo treatment for lower urinary tract symptoms.
- Long-term evidence (beyond two to six years) on all four treatments is still lacking. Head-to-head comparative trials of these newer treatments are also needed.
- Limited short-term cost analyses suggest that some of the less invasive treatments are less costly than conventional treatments, such as TURP. Long-term cost-effectiveness analyses are needed to determine if potential cost savings with these less invasive treatments can be realized.

## Background

The prostate is a small male reproductive gland that surrounds part of the urethra, just below the bladder.<sup>1</sup> BPH, or an enlarged prostate, becomes more common as people age.<sup>2,3</sup> It is estimated to affect more than 50% of people with prostates in their 60s and more than 70% of those in their 70s and 80s.<sup>4-6</sup> With Canada's aging population, it is expected that more people will seek health care advice and treatment for lower urinary tract symptoms caused by BPH.<sup>7,8</sup>

In BPH, the enlarged prostate, puts pressure on the urethra and bladder. This can cause lower urinary tract symptoms, such as:

- urinary retention due to bladder outlet obstruction
- dysuria (pain or difficulty urinating), reduced flow of urine, dribbling, or incomplete emptying of the bladder

- increased urgency or frequency of urination
- nocturia (the need to urinate frequently during the night)
- urinary incontinence.<sup>6,7</sup>

In some people, BPH may cause no troublesome symptoms while others may experience one or more symptoms, and symptoms may fluctuate.<sup>6,9</sup> Although it is not cancerous, BPH can progress and the enlarged prostate may eventually cause chronic urinary retention, recurrent urinary tract infections, bladder stones, bleeding, or in severe cases, kidney failure.<sup>1,10</sup> Lower urinary tract symptoms due to BPH can also affect quality of life through disrupted sleep, sexual dysfunction, and depression.<sup>2,6,11-13</sup>

Current surgical treatments for lower urinary tract symptoms due to BPH, such as TURP, carry a risk of permanent adverse effects, including ejaculatory dysfunction (in particular, retrograde

ejaculation, when the semen is emitted backwards into the bladder) and urinary incontinence.<sup>14</sup> As the prevalence of BPH increases with age, many of those affected may have other health conditions or frailty which means they are more at risk for adverse events from drug therapies and surgical procedures.<sup>1,15</sup>

The 2018 update to the Canadian Urological Association guidelines on BPH includes several procedures that are less invasive than surgical treatments.<sup>7</sup> These may offer more appealing treatment options for some and alternatives for older individuals who cannot undergo surgery.

## The Technologies

Various drug and non-drug treatment options are available to manage lower urinary tract symptoms caused by BPH. Which treatment is most appropriate for a particular patient depends on several factors, including the patient's preferences, sexual functioning, comorbidities, the severity and types of symptoms due to BPH, the size and shape of the enlarged prostate, the treatment options available locally, and the clinician's experience with a particular technology.<sup>10,17</sup> Other considerations are the expected long-term durability of the treatment, potential level of symptom relief, and the risk for particular adverse events – which also differ between the various treatment options.

This bulletin focuses on four new treatments for lower urinary tract symptoms due to BPH.

### Prostatic urethral lift – UroLift (Teleflex Incorporated / NeoTract Inc., Pleasanton, CA)

The prostatic urethral lift uses small, suture-like implants that are inserted using a single-use delivery device. The probe end of the device is inserted into the urethra. When deployed, a fine needle attaches one end of the UroLift implant to a lobe of the prostate and the other to the prostatic urethra.<sup>18,19</sup> The implants consist of a nitinol tab and stainless steel end piece, connected by a polyethylene terephthalate (polyester) monofilament.<sup>18,19</sup> Once implanted, the devices compress and hold back the lobes of prostatic tissue to prevent obstruction of the urethra.<sup>18,20,21</sup> No cutting or ablation of tissue is involved.<sup>22</sup>

The urethral lift procedure is performed by a urologist and it may be performed in either a hospital or an outpatient clinic.<sup>18</sup> Typically four or five implant devices are used for each procedure, but patients with larger prostates or those with median lobes may require additional implants.<sup>18,23</sup> The UroLift implants are intended to be left in place permanently, but some individuals require follow-up procedures for additional implants, or some patients may require procedures to remove the implants.<sup>18</sup>

### Water vapour thermal therapy – Rezūm (NxThera / Boston Scientific, Marlborough, MA)

The Rezūm water vapour thermal system uses convective energy in the form of steam to ablate prostate tissue.<sup>24</sup> The steam is produced by a radiofrequency generator and applied through the wall of the urethra using a single-use delivery device (similar to a cystoscope) with a retractable treatment needle that emits the water vapour.<sup>9,20,24,25</sup> One delivery device is used for each patient's treatment, regardless of the size of the prostate.<sup>24</sup> The water vapour is applied in short (typically nine second) injections to prostate tissue near the urethra. As the steam-treated tissue dies and is absorbed by the body, the size of the prostate is reduced and lower urinary tract symptoms improve over a period of several weeks.<sup>9,20,26</sup> The thermal energy is confined to the prostate, reducing the risk of injury to adjacent areas, such as the bladder, rectum, or urinary sphincter.<sup>20,26</sup> Water vapour treatments are performed by a urologist in an outpatient clinic, and the procedure can be repeated in the future, if necessary.<sup>20,24</sup>

### Prostatic artery embolization

Prostatic artery embolization uses tiny embolization agents (microspheres) made of trisacryl gelatin, polyvinyl alcohol, or biodegradable agents (such as polylactic-co-glycolic acid [PLGA] sed in Ekobi microspheres) that are injected into the prostatic arteries. The microspheres are delivered into selected blood vessels through a catheter inserted into the femoral artery in the groin or the radial artery in the wrist.<sup>20,27</sup> The microspheres block the blood supply to the prostate, causing tissue death and reducing the size of the prostate.

Before the procedure, MRI may be done to ensure cancer is not present, and a pelvic computed tomography (CT) angiography is conducted to map the blood flow to the prostate and ensure the patency of the blood vessels.<sup>20,28</sup> The embolization procedure is performed by an interventional radiologist, in consultation with a urologist, and both specialists jointly determine a patient's suitability for the procedure. The procedure is carried out in an interventional radiology suite.<sup>29</sup>

### Aquablation – AquaBeam (Procept BioRobotics, Redwood City, CA)

Aquablation is an endoscopic surgical procedure that removes prostatic tissue using a high-velocity, heat-free, saline waterjet. The treatment is delivered by a single-use hand piece inserted through a reusable, rigid cystoscope.<sup>30,31</sup> The procedure is performed by a urologist in the operating room. During the procedure, robotic surgical assistance and real-time imaging guidance is used (cystoscopy and transrectal ultrasound).<sup>20,30,32</sup>

## Regulatory Status

All four of the technologies discussed in this bulletin have Health Canada licences allowing them to be marketed in Canada.

- UroLift (Teleflex Incorporated / NeoTract Inc.) – Health Canada licence in September 2011.<sup>33</sup>
- Rezūm (NxThera Inc. / Boston Scientific) – Health Canada licence in September 2018.<sup>24,33,34</sup>
- Ekobi Embolization Microspheres (formerly Occlusin Embolization Microspheres, IMBiotechnologies Ltd.) – Health Canada licence in October 2018, indicated for the treatment of hypervascular tumours, uterine fibroids, and BPH.<sup>35</sup> Other embolization products that have Health Canada licences include: Embosphere microspheres (Merit Medical),<sup>36</sup> PVA foam embolization particles (Cook, Inc.),<sup>37</sup> and Embozene Microspheres (Varian Medical Systems).<sup>38</sup>
- AquaBeam (Procept BioRobotics) – Health Canada licence in September 2017.<sup>39</sup>

## Cost

A 2019 US review cited annual drug costs of monotherapies for BPH ranging from US\$1,333 to US\$1,566, with combination drug therapies costing up to US\$2,843.<sup>15</sup> The authors noted that less invasive treatments were initially more costly than drug therapies, but over the course of several years they could be more cost-effective, and these could be considered a first-line treatment option for appropriately selected patients.<sup>15</sup> In Canada, drug therapies may be less costly than in the US. For example, in Alberta the annual cost for four of the drugs commonly prescribed for BPH ranges from \$100 to \$240.<sup>40</sup> However, another recent Canadian estimate stated an annual cost of \$1,000 per year for multi-drug, combination BPH drug therapies.<sup>41</sup>

A 2019 US study, funded by NxThera, compared costs of drug therapies to surgical and office-based treatments for BPH, including prostatic urethral lift and thermal water vapour ablation.<sup>42</sup> Compared with an estimated one-year cost for combination drug therapy (US\$1,434), water vapour ablation (US\$830) reached cost equivalence in about six months, while prostatic urethral lift (US\$3,779) reached cost equivalence to drug therapy in about two and a half years. Cost equivalence time for prostatic urethral lift was similar to that for photoselective laser vaporization and TURP.<sup>42</sup> These cost estimates did not include the costs of preoperative procedures (such as cystoscopy, ultrasound, office visits), or post-operative follow-up costs (including treatment of complications).<sup>42</sup>

## Prostatic urethral life (UroLift)

A 2018 US news item reported a cost of between US\$700 and US\$1,000 (approximately C\$900 to C\$1,300) for each UroLift implant (suture) and single-use delivery device.<sup>43</sup> A similar estimate was provided by a Canadian clinical expert, who noted that each UroLift implant costs from \$1,000 to \$1,300 (Dr. Dean Elterman, University of Toronto, Toronto, ON: personal communication, 2019 Dec 17). Most prostatic urethral lift procedures require at least four implants and more implants are needed for those with median lobes or larger prostates.<sup>18,23</sup> A US modelling study of the costs of six different BPH treatments cited a per-procedure cost (with four UroLift implants) of US\$6,230 (approximately C\$8,200) based on 2016 US Center for Medicare and Medicaid Services data.<sup>44</sup>

Guidance from NICE in the UK on prostatic urethral lift treatment anticipated that, despite the additional cost of the implants, the UroLift system could offer cost savings over surgical treatment if performed as an outpatient procedure, and then because fewer post-procedure follow-up visits may be needed.<sup>18</sup>

## Water vapour thermal therapy (Rezūm)

In Canada, the Rezūm generator costs \$99,500 and the single-use delivery device costs \$3,500 (Darwin Barthelemy, Boston Scientific Canada, Calgary, AB: personal communication 2019 Dec 16). In a 2018 NICE brief on Rezūm, the expected lifespan of the generator was estimated to be from five to seven years.<sup>45</sup> Updated UK NICE draft guidance includes an economic model that compares Rezūm with TURP, photoselective vaporization, holmium laser enucleation, and UroLift.<sup>46</sup> During a four-year time frame, Rezūm was determined to be cost-saving (by more than £497 per procedure, or approximately C\$850) compared with TURP, holmium laser, and UroLift. Rezūm was cost-neutral when compared with photoselective vaporization, if both procedures are performed as day surgeries.<sup>46</sup>

Costs in the US may not be generalizable elsewhere; however, the US modelling study found water vapour thermal therapy to be less costly and to have fewer adverse events than other minimally invasive therapies, including UroLift.<sup>44,47</sup>

## Prostatic artery embolization

According to the Canadian manufacturer, IMBiotechnologies, the Ekobi biodegradable microspheres manufacturer's suggested retail price for the product is \$500 per vial. Most prostatic artery embolization procedures use one vial, but, depending on the size of the prostate and the individual's vasculature, some procedures may use two vials (Michael W. Stewart, IMBiotechnologies Ltd., Edmonton, AB: personal communication, 2019 Oct 10).

A 2019 Canadian study, using Ontario Case Costing Initiative costs, calculated the average total hospital costs of prostatic artery embolization as \$3,829.<sup>48</sup> (Note that the costs did not include physician fees or non-hospital costs, but did include hospital costs up to 30 days post-procedure.) The authors reported that these costs were less than average costs for both photoselective laser vaporization (GreenLight laser therapy) of the prostate (\$5,719) and TURP (\$5,034).<sup>48</sup> However, another Canadian cost analysis that compared the costs of photoselective vaporization with TURP found that laser vaporization had lower costs (\$3,836 for photoselective vaporization, \$4,963 for TURP, and \$4,978 for bipolar TURP).<sup>49</sup> Length of stay was shorter with prostatic artery embolization (one day), compared with photoselective vaporization (1.55 days) and TURP (1.63 days).<sup>48</sup> The authors noted that the durability of prostatic artery embolization is yet unknown, and this may affect future cost estimates.<sup>48</sup>

## Aquablation (AquaBeam)

Little cost information on the AquaBeam system or the aquablation procedure was identified. A Canadian clinical expert estimated the cost of the AquaBeam system as \$300,000, with the single-use handpiece used for each procedure costing \$2,500 (Dr. Dean Elterman, University of Toronto, Toronto, ON: personal communication, 2019 Dec 17). Information on the PROCEPT BioRobotics website indicates a current Medicare physician payment of US\$4,020, plus additional hospital inpatient charges (not costed), and an add-on new technology payment of US\$1,250 (a total of approximately C\$7,000).<sup>50</sup> A 2017 UK newspaper article reported the cost of the aquablation procedure at a private clinic as around £9,000 (C\$15,400).<sup>51</sup> As the procedure is performed in an operating room, under general anesthesia, and not as an outpatient procedure, overall costs will likely be higher with aquablation than with the other three technologies discussed in this bulletin.

## Who Might Benefit?

Approximately 6,800,000 Canadian men are 50 years of age and older.<sup>52</sup> Of these, an estimated 2,578,000 have moderate-to-severe lower urinary tract symptoms due to BPH;<sup>4</sup> many of whom will not seek treatment until symptoms significantly affect their quality of life.<sup>3</sup> Based on US estimates, approximately 60% (1,500,000) of Canadians with lower urinary tract symptoms due to BPH will seek health care treatment for these symptoms. Of those who seek treatment, about 54% (810,000) receive first-line drug treatments, such as alpha blockers, or try but discontinue drug therapies and return to watchful waiting.<sup>2</sup> Another 35% (525,000) of those seeking treatment opt for watchful waiting only.<sup>2</sup> Annually, 1% to 2% of those with BPH may

need surgical interventions such as TURP, laser procedures, or prostatectomy.<sup>2,15,18</sup>

As of 2011, in Canada, approximately 20,000 TURPs were performed annually for lower urinary tract symptoms due to BPH.<sup>8</sup> About 1,600 laser procedures for BPH were also performed that year.<sup>8</sup> Prostatectomy is one of the 10 most common surgical procedures across Canada, with more than 25,500 procedures performed in 2017-2018 (this number includes prostatectomies for both prostate cancer and for BPH).<sup>53</sup>

The manufacturer submission to the UK NICE costing statement on prostatic urethral lifts noted that about 25% of those eligible for surgical interventions for BPH may be suitable for UroLift implants.<sup>54</sup> Clinical experts commenting on the potential patient population for Rezūm in the UK had various estimates, ranging from 15% to 20% of patients with bothersome lower urinary tract symptoms could be eligible, or 50% of those on BPH drug therapies, or from 50% to 100% of those eligible for TURP.<sup>55</sup> No estimates of the potential numbers of those suitable for prostatic artery embolization or aquablation were found.

## Current Practice

Determining the severity of lower urinary tract symptoms, their impact on quality of life (bother), and patient preferences are key considerations in selecting the most appropriate treatment.<sup>7</sup> Those with symptoms of BPH that are not significantly affecting their quality of life or causing urinary tract complications may opt for watchful waiting and behavioural changes. Behavioural changes include: weight loss, exercise, smoking cessation, reducing consumption of fluids before bedtime, reducing consumption of diuretics such as caffeine and alcohol, sitting instead of standing while urinating, and double voiding to more completely empty the bladder.<sup>2,56-58</sup>

Drug therapies are usually the first-line treatment for mild to moderate “bothersome” lower urinary tract symptoms of BPH that cannot be managed through behavioural changes.<sup>11,56,59</sup> Drug therapies include monotherapies, such as alpha blockers or anti-cholinergics.<sup>7,56,59</sup> For those with more severe symptoms and/or larger prostates, a combination of drug therapies may be recommended.<sup>56</sup>

Some drug therapies may prevent progression of BPH, without significantly improving symptoms, and other drugs may take months for symptom relief to take effect.<sup>42</sup> Consequently, long-term compliance with drug therapies tends to be low.<sup>15</sup> The drug therapies also have various adverse effects and many people discontinue treatment as a result.<sup>56</sup> Estimates are that that up to 60% of patients stop taking BPH-related drugs within the first

year.<sup>13,60</sup> Potential adverse drug effects include low blood pressure, dizziness, ejaculatory dysfunction, erectile dysfunction, retrograde ejaculation, decreased libido, and depression.<sup>15,56,60</sup>

Individuals with additional or more severe symptoms, test results that suggest other conditions may be present, those who have a younger age of onset (before age 45), or those for whom initial therapies have failed, may need to be referred to a urologist.<sup>6</sup> Surgical treatments may be considered if drug treatments have not improved symptoms, symptoms have progressed, or BPH has caused complications, such as urinary retention, recurrent urinary tract infections, bladder stones, kidney dysfunction or bladder obstruction.<sup>7,13,56</sup> Surgical treatments include TURP, photoselective laser vaporization of the prostate (GreenLight laser therapy), holmium laser enucleation of the prostate (HoLEP), thulium laser enucleation and vapoenucleation (ThuLEP), or prostatectomy (surgical removal of the prostate gland using various techniques).<sup>29,61</sup> Potential adverse events associated with these procedures include urinary incontinence, sexual dysfunction, strictures, bleeding, and infection.<sup>29</sup>

Holmium laser enucleation has been found to be more effective than TURP in alleviating lower urinary tract symptoms in patients with very large glands, and it has been found to have a lower risk of adverse events.<sup>62</sup> However, it has a steep learning curve.<sup>30,61,63,64</sup> TURP is still generally regarded to be the “gold standard” for the treatment of small to moderate-sized prostates (< 80 grams).<sup>30,65,66</sup>

Larger prostates (> 80 grams) are more difficult to treat, and options may be limited to laser treatments or prostatectomy.<sup>11,41,67</sup> In Canada, few urologists have the training and expertise needed to perform holmium laser enucleation, which may result in long wait times for this treatment, or in more patients undergoing prostatectomy.<sup>41</sup> Photoselective vaporization of the prostate (GreenLight laser) is more widely available in Canada than holmium laser enucleation, and it can also be used to treat large prostates (Dr. Dean Elterman, University of Toronto, Toronto, ON: personal communication, 2019 Dec 17).<sup>68</sup>

## Summary of the Evidence

The supporting 2019 [Rapid Response report with Critical Appraisal](#) reviewed recent comparative clinical effectiveness information on these less invasive therapies.<sup>16</sup> Four systematic reviews, two randomized controlled trials, and one retrospective comparative study were identified in the rapid review that addressed the clinical effectiveness and safety of less invasive techniques for the treatment of lower urinary tract symptoms in patients with BPH.<sup>16</sup> No head-to-head studies between the newer therapies were identified. All of the studies identified and included

in the Rapid Response compared the newer treatments with TURP. As the Rezūm water vapour thermal therapy has only been directly compared with sham treatment and not to another active treatment, no studies relevant to the procedure were included in the Rapid Response, however, studies comparing Rezūm with sham or drug therapies have been included here. Additional studies, published after the Rapid Response was prepared, are also included in this bulletin. These studies have not been critically appraised.

The [International Prostate Symptom Score \(IPSS\)](#) is a validated questionnaire that is often used to determine the severity of lower urinary tract symptoms of BPH and their impact on quality of life.<sup>2,6,44</sup> A score of seven or less on the IPSS scale indicates mild symptoms; a score of eight to 19 indicates moderate symptoms, and a score of 20 to 35 indicates severe lower urinary tract symptoms.<sup>2,7</sup> A decrease in score of at least three points is considered to be a meaningful clinical improvement.<sup>2</sup>

In an effort to summarize key findings from the literature as simply as possible we have considered mainly IPSS symptom and quality of life scores, impact on sexual function, and adverse events in the sections that follow. Table 1 provides a summary of other information from the most recent studies that highlight further differences and similarities between the treatments.

### Prostatic urethral lift (UroLift)

The [2019 CADTH Rapid Response Report](#) included two systematic reviews<sup>17,69</sup> and one randomized controlled trial<sup>70</sup> that compared prostatic urethral lift with TURP at 12 and 24 month follow-up.<sup>16</sup> Although TURP was more effective in relieving lower urinary tract symptoms, prostatic urethral lift was superior in maintaining or improving sexual function, and in speed of recovery post-procedure.<sup>16</sup> Improvements in quality of life were not significantly different between the two treatments.<sup>16</sup>

### Other information

Another recent assessment on prostatic urethral lifts include a 2019 ECRI Institute Product Brief.<sup>19</sup> The ECRI brief concluded that UroLift improved lower urinary tract symptoms and quality of life, and that, unlike TURP, it did not affect ejaculatory function (as of two-year follow-up).<sup>19</sup> ECRI noted the need for randomized controlled trials comparing UroLift with TURP to determine UroLift’s long-term effectiveness and its effectiveness for those with median prostatic lobes.<sup>19</sup>



A 2019 paper reported two-year follow-up of a non-comparative study of 86 patients who received prostatic urethral lifts at five centres in Germany.<sup>71</sup> The IPSS and quality of life scores improved by 51% and 52% respectively at follow-up (45 patients [53%] were not available for the full two-year assessment).<sup>71</sup>

MedLift, a US FDA extension of the L.I.F.T. study, included participants with median prostatic lobes who received prostatic urethral lifts.<sup>23</sup> In the 2019 report of 12-month follow-up for the 45 MedLift participants, no new cases of erectile or ejaculatory dysfunction were reported.<sup>23</sup> The MedLift investigators reported that participants' quality of life was improved by more than 60% at 12 months.<sup>23</sup>

## Water vapour thermal therapy (Rezūm)

As no studies comparing water vapour thermal therapy to TURP or other active BPH treatments were identified, information regarding this treatment was not included in the 2019 CADTH Rapid Response Report.<sup>16</sup>

### Other information

To date the largest study of water vapour thermal therapy is a multi-centre US randomized controlled trial that compared water vapour (n = 135) with sham treatment (n = 61) for moderate-to-severe lower urinary tract symptoms due to BPH.<sup>72</sup> The original randomized controlled trial had a three-month follow-up — which was followed by a crossover for those who received sham — and a further four years of data collection. At the three-month follow-up, IPSS symptoms were reduced by 50% in the water vapour group, compared with 20% in the sham treatment group (authors noted that the sham treatment result may have been a temporary effect of the rigid cystoscopy procedure).<sup>72</sup> Clinical improvement for those in the initial water vapour group was similar at four years to that seen at three months (46.7%).<sup>72</sup> No negative impact on sexual function (libido, erectile or ejaculatory function) was reported.<sup>72</sup> The investigators noted that quality of life scores improved over the four years of the study.<sup>72</sup>

The NICE 2018 briefing on water vapour treatment for BPH concluded that water vapour treatment was effective in improving lower urinary tract symptoms.<sup>45</sup> The main uncertainties were the lack of studies directly comparing Rezūm to TURP or other BPH treatments.<sup>45</sup> An interventional procedure overview of evidence and guidance, issued by NICE in 2018, also concluded there was adequate evidence to support the use of water vapour treatment, but that it should only be performed by a urologist with training in the procedure and under the initial guidance of another clinician with experience with the procedure.<sup>73</sup> The NICE interventional procedure overview on water vapour thermal therapy noted that 3% of those who received the procedure reported ejaculatory

dysfunction post-procedure (e.g., decreased ejaculate, anejaculation, or retrograde ejaculation), and 3% reported erectile dysfunction.<sup>73</sup>

A 2018 US study, that compared 136 patients treated with water vapour therapy to patients treated with BPH drug therapies in an earlier US study, found that IPSS symptom scores improved by approximately 50% over three years in the patients who received water vapour therapy.<sup>74</sup> This was a greater improvement in IPSS than that achieved with single drug therapies over three years, but improvement was similar to that achieved with combination drug therapies. However, over the three-year period, progression of BPH was five times higher in those receiving single or combination drug therapies, than in those who received water vapour therapy.<sup>74</sup> The authors comment that using drug therapies to delay other interventions for BPH symptoms may result in older patients with larger prostates and more comorbidities, who consequently would be at higher risk of needing invasive procedures.<sup>74</sup>

## Prostatic artery embolization

The 2019 CADTH Rapid Response Report appraised the evidence from two systematic reviews<sup>75,76</sup> and one retrospective non-randomized study<sup>77</sup> on prostatic artery embolization.<sup>16</sup> Results were mixed for various clinical outcomes, but overall, they favoured TURP for symptom improvements, whereas participants who underwent prostatic artery embolization had fewer complications.<sup>16</sup>

### Other information

A 2019 ECRI Institute brief on prostatic artery embolization using the Embosphere microspheres included six studies that reported follow-up of at least one-year.<sup>78</sup> Overall, the brief concluded that prostatic artery embolization reduced lower urinary tract symptoms and improved quality of life, but that better quality controlled trials with longer follow-up are needed.<sup>78</sup>

A 2019 Swedish health technology assessment that compared prostatic artery embolization with TURP concluded that embolization could be performed as a day surgery procedure, using local anesthesia — unlike TURP which requires hospitalization and spinal anesthesia (this information is based on an English summary of the Swedish report).<sup>79</sup> The assessment highlighted that the training and skills of the interventional radiologists were critical, and that embolization should only be provided at a centre of expertise and with the collaboration of urologists. Authors also recommended the need for patient registries to track outcomes and adverse events. Prostatic artery embolization was deemed most relevant for elderly patients with comorbidities who cannot undergo spinal or general anesthesia,

and for those with large prostates.<sup>79</sup> A 2019 study of 48 patients treated with prostatic artery embolization in Switzerland, also noted better outcomes in patients with large, rather than small, prostates.<sup>80</sup>

The 2018 UK NICE guidance on prostatic artery embolization noted that the safety and efficacy of the various embolization agents used in the published studies could differ.<sup>27</sup> Moreover, the techniques used for the procedure have changed and outcomes with the newer “PERFecTED technique” have improved outcomes over those reported in older studies.<sup>27,81</sup> The NICE guidance also noted that reporting of rates and severity of adverse events varied across the studies.<sup>27</sup>

Real-world evidence is available from the UK Register of Prostate Embolization (UK-ROPE).<sup>81</sup> The registry provided information on 305 patients who underwent prostatic artery embolization (216 patients) and TURP (89 patients) at 17 UK centres.<sup>81</sup> At 12-month follow-up, prostatic artery embolization had improved IPSS lower urinary tract symptom scores by an average of 10 points, compared with an average of 15 points for TURP.<sup>81</sup> Average embolization procedure time (in the operating room) was 144 minutes, and average radiation screening time was 38 minutes.<sup>81</sup> Rates of retrograde ejaculation in the patients who received embolization were about half that of those who received TURP.<sup>81</sup> Quality of life outcomes were similar for both treatments.<sup>81</sup> Embolization enabled a faster return to normal activities — an average of five days for embolization versus 14 days for TURP.<sup>81</sup> Most embolization procedures were performed on an outpatient basis, whereas most TURP procedures required at least one or two nights hospital stay.<sup>81</sup>

A 2019 UK case series report noted an average fluoroscopy time of 36 minutes — which was shorter than that reported in other studies. This was due to avoidance of cone-beam CT and other techniques to minimize radiation exposure.<sup>82</sup>

Results from the UK-ROPE registry found patient retreatment rates after embolization were 5% (up to 12 months), and 15% after 12 months, for a total retreatment rate of 20% at two years.<sup>81</sup> In addition, 23% of those taking BPH drug therapies before undergoing embolization treatment were still taking them three months after the procedure.<sup>83</sup>

Currently, Canadian and US urological association guidelines do not recommend the use of prostatic artery embolization until further evidence is available.<sup>7,11,21,81</sup> However, based on a review of studies that included more than 2,200 patients, a 2019

international interventional radiology society position statement, endorsed by the Canadian Association for Interventional Radiology, recommended that prostatic artery embolization is “an acceptable minimally invasive treatment option for appropriately selected men with BPH and moderate-to-severe LUTS” (lower urinary tract symptoms).<sup>84</sup> The international interventional radiology society position statement concluded that sexual function is better after prostatic artery embolization compared with after TURP.<sup>84</sup> Erectile function was either unchanged or slightly better in patients who underwent embolization, and ejaculatory dysfunction occurred much less often than with TURP or prostatectomy.<sup>84</sup>

### ***Biodegradable microspheres for prostatic artery embolization — emerging evidence***

Ekobi biodegradable microspheres, developed in Edmonton, can be visualized using ultrasound, allowing treatment to be monitored. Results of a pilot study of Ekobi microspheres in 10 participants with moderate-to-severe lower urinary tract symptoms due to BPH was presented at the 2019 Society of Interventional Radiology conference.<sup>85</sup> Six participants received bilateral prostatic artery embolization, and four received unilateral treatment. The average IPSS score was 24.2 at baseline, and this improved to 15.1 at one-year follow-up. Quality of life improved in nine of the 10 participants at one-year follow-up, with no reports of adverse events or negative impact on sexual function.<sup>85</sup> Full study results are not yet available.

### **Aquablation (AquaBeam)**

The [2019 CADTH Rapid Response](#) included four reports<sup>86-89</sup> (including subgroup analyses) of the WATER randomized controlled trial that compared aquablation with TURP at 17 centres in the US, UK, Australia, and New Zealand.<sup>16</sup> At six and 12-month follow-up there were no significant differences in clinical outcomes or quality of life between the two procedures.<sup>16</sup> However, for those with larger prostates or those with a median prostatic lobe, clinical symptom improvement at six months was better with aquablation.<sup>16</sup>

### ***Other information***

Other recent assessments and systematic reviews on aquablation include a 2019 ECRI Institute brief,<sup>31</sup> a 2019 Cochrane systematic review,<sup>1</sup> and a 2019 European systematic review.<sup>90</sup> The ECRI Institute brief concluded the evidence for aquablation was somewhat favourable, and that symptom relief and quality of life improvements at two years were similar between aquablation and TURP.<sup>31</sup>

**Table 1: Summary of Additional Information on the Four Minimally Invasive Treatments for BPH**

	Prostatic urethral lift (UroLift)	Water vapour thermal therapy (Rezūm)	Prostatic artery embolization	Aquablation (AquaBeam)
Prostate size / median lobe <sup>a</sup>	Small-medium + median lobe <sup>20,95</sup>	Small-large (UK) / small-medium (US) + median lobe <sup>b24,26,55</sup>	Small-large + median lobe <sup>20</sup>	Small-large + median lobe <sup>64,67</sup>
Professional to perform the procedure	Urologist	Urologist	Interventional radiologist (with Urologist)	Urologist
Anesthesia	Local plus oral sedation or general <sup>96</sup>	Local plus sedation, prostate block, or IV sedation <sup>72</sup>	Local + sedation <sup>20,48</sup>	Spinal or general <sup>20, 67</sup>
Procedural time (approximate) <sup>c</sup>	25 minutes <sup>97</sup>	20 minutes <sup>26,45</sup>	2 hours <sup>20,81</sup>	35 minutes (aquablation resection time 8-9 minutes) <sup>41 92</sup>
Outpatient (day procedure) / Inpatient	Outpatient <sup>26</sup>	Outpatient <sup>24,26,72</sup>	Outpatient <sup>20</sup>	Inpatient <sup>22,30,98</sup>
Average length of stay	2.4 to 4 hours hours <sup>23,97</sup>	Not reported	< 1 day <sup>48,82</sup> ; 71% performed as outpatients in UK registry study <sup>81</sup>	1.3 days <sup>41</sup>
Typical duration of catheterization post-procedure	0 to 1.2 days <sup>23,71,99,100</sup>	3 or more days <sup>24,26,73</sup>	< 1 day (only until trial of voiding post-procedure) <sup>101</sup>	1-4 days <sup>41, 67,102</sup>
Learning curve	Short <sup>22</sup>	Short <sup>72</sup>	Steep (after training and assessment, a learning curve of at least 10 to 20 cases) <sup>29,81</sup>	Short <sup>30,67</sup>
Longest reported follow-up	5 years <sup>26</sup>	4 years <sup>72</sup>	6 years <sup>84,103</sup>	2 years <sup>104</sup>
Retreatment rates	11% (at 1 year); 13.5% (at 5 years), & 10.7% of patients taking BPH drug therapies (at 5 years) <sup>99,105</sup>	4.4% surgical retreatment and 5.2% of patients taking BPH drug therapies (up to 4 years) <sup>72</sup>	5% (up to 12 months), 15% after 12 months, for a total rate of 20% at 2 years. <sup>81</sup> 23% of those taking BPH drug therapies before embolization still taking them at 3 month <sup>83</sup>	4.3% (at 2 years) <sup>104</sup>

Note: this table is based on information extracted from recent studies discussed further in the report, but it is not based on a systematic review of all the evidence on these treatments. Local practice also varies and this may affect aspects such as type of anesthesia used, post-procedure catheterization, and length of stay.

<sup>a</sup> Small-medium = 30 g to 80g; Large = > 80 g.

<sup>b</sup> Some studies included larger prostates.

### **WATER Study**

The European systematic review covered the literature to July 2019 and included results from 16 studies with a total of 446 patients, the WATER trial to two-years follow-up, and several single and multi-centre non-randomized studies and subgroup analyses.<sup>90</sup> The reviewers concluded that aquablation and TURP achieved similar clinical outcomes, but that aquablation had fewer adverse events and lower rates of anejaculation.<sup>90</sup> However, a commentary on the WATER study noted the lack of evidence of benefit for other sexual outcomes.<sup>91</sup>

### **WATER II study**

The WATER II study of aquablation treatment of larger prostates did not include a comparator treatment.<sup>67</sup> Most patients (82%) in WATER II received spinal anesthesia, and 18% received general anesthesia.<sup>67</sup> A 2019 paper reported on three-month follow-up of 19 patients, treated with aquablation at three Canadian centres in the WATER II study.<sup>41</sup> Average IPSS scores improved from 21.2 at baseline to 5.0 at three-months post-treatment.<sup>41</sup> Average quality-of-life scores improved from 4.3 at baseline to 1.5 at three months, but 32% of patients reported persistent ejaculatory dysfunction.<sup>41</sup>

At 12-month follow-up, among participants who were sexually active at baseline, 81% maintained normal ejaculatory function and 19% reported ejaculatory dysfunction.<sup>92</sup> Overall sexual function scores decreased slightly from baseline to 12 months; no new cases of erectile dysfunction were reported.<sup>92</sup> Persistent ejaculatory dysfunction was reported by 32% of Canadian patients in the subgroup analysis.<sup>41</sup>

The NICE guidance on aquablation, issued in September 2018, was based on earlier reports from the WATER randomized controlled trial, one single arm trial and three smaller case series studies.<sup>93</sup> Outcomes and adverse events from these studies are described in detail in the interventional procedures overview for the guidance.<sup>94</sup> The overview notes that the studies used both the first and second generation of the aquablation system, and that safety and efficacy may differ.<sup>94</sup> The guidance concluded that aquablation did not appear to raise major safety concerns, but that due to limited evidence of efficacy, it should be used with special considerations for informed patient consent, and audit and further research to collect long-term follow-up information and reintervention rates.<sup>93</sup>

## Safety

Potential adverse events from TURP and other current surgical treatments for BPH include bleeding, incontinence, urethral strictures, and sexual dysfunction.<sup>27</sup> The [CADTH Rapid Response](#) concluded that “safety outcomes favoured minimally invasive surgical techniques over TURP.”<sup>16 27</sup>

### Prostatic urethral lift (UroLift)

Earlier NICE guidance on urethral lifts, published in 2015, and more recent studies have noted mainly mild, temporary, adverse events with the UroLift implants, including dysuria and hematuria (blood in the urine).<sup>18,23,71</sup> Urinary incontinence was less common after UroLift (5%) compared with TURP (11%).<sup>18</sup> NICE clinical experts advised that incrustation of the implants could occur if they are placed too close to the bladder and that this would require removal of the implants.<sup>18</sup> The 2019 ECRI Institute brief on UroLift noted a recall of some devices because of failure of the delivery device to deploy properly.<sup>19</sup> The US FDA MAUDE database of adverse events includes reports that may be associated with UroLift treatment, such as infection, bleeding, urinary retention, device misplacement, malfunction, fragmentation or migration.<sup>106</sup>

A recent US review of device malfunctions and complications for TURP, holmium laser enucleation, photoselective laser vaporization and UroLift concluded that a little more than 40% of adverse event reports in the MAUDE database were due to operator error.<sup>107</sup> (The MAUDE database does not capture all

adverse events that occur with any given device.<sup>107</sup>) The US FDA is currently reviewing concerns regarding biological responses to metal in implanted medical devices.<sup>108,109</sup> Although the UroLift implants are not specifically mentioned, long-term monitoring of patients for possible immune reactions to the implants may be warranted.

### Water vapour thermal therapy (Rezūm)

The four-year report on the main study of water vapour thermal therapy reported adverse events of mild to moderate severity that are typically associated with cystoscopy, including pain or dysuria (16.9%), hematuria (11.8%), frequency or urgency of urination (5.9%), acute urinary retention (3.7%), and urinary tract infection (3.7%).<sup>72</sup> All adverse events were either treated or resolved without needing treatment within three weeks.<sup>72</sup>

ECRI Institute’s brief on the Rezūm system noted one US FDA device alert due to possible needle breakage, and a 2018 recall of some devices.<sup>9</sup> The US FDA MAUDE database of adverse events includes reports that may be associated with the treatment, including pain, urinary retention, bleeding, retention of necrotic tissue, and urinary tract infection. There were also several reports of the delivery device malfunctioning.<sup>110</sup>

A 2019 paper described four urologists’ experience with Rezūm.<sup>24</sup> The authors noted the possibility of retained tissue post-procedure that could lead to bladder stone formation.<sup>24</sup> Based on their experience with the technology, the authors reported that residual calcified tissue was confirmed in less than 1% of their patients.<sup>24</sup>

The 2018 NICE interventional procedure overview noted adverse events reported in the randomized controlled trial and case series they reviewed included ablation to tissue outside of the prostate reported in one patient; blood in the semen (7%) or in the urine (13% to 14%); urinary tract infection (suspected in 4% to 20%); dysuria (17% to 22%); urinary retention (4% to 14%), urinary incontinence (4%); and urinary frequency (7%) and urgency (6%).<sup>73</sup> In addition, 2% of patients experienced urethral stricture and one patient had a bladder neck contracture.<sup>73</sup>

### Prostatic artery embolization

The [2019 CADTH Rapid Response](#) concluded that the incidence of complications for the patients who underwent TURP or prostatectomy was double (63.8%) that of those who underwent prostatic artery embolization (31.1%).<sup>16</sup>

The 2019 ECRI Institute brief on prostatic artery embolization with the Embosphere microspheres noted that the published studies reported minor adverse events, such as transient pain, urinary incontinence, dysuria, and fever.<sup>78</sup> The brief noted no US

recalls or FDA MAUDE adverse events reports on the use of the Embosphere microspheres for prostatic artery embolization; however, they cautioned that microspheres have a potential for migration and longer-term follow-up studies are needed.<sup>78</sup>

A joint 2019 position statement issued by Canadian, European, and Asian interventional radiology associations summarized the adverse events associated with prostatic artery embolization.<sup>84</sup> These included transient post-procedural pain, dysuria, and frequency of urination, acute urinary retention requiring temporary catheterization (in 2.5% to 4.6% of patients), and urinary tract infections (in 2.6% to 7.6% of patients). The position statement noted that major complications were reported for six of 2,000 patients (0.5%) included in the studies to 2018.<sup>84</sup>

The 2018 NICE guidance overview noted adverse events reported in the literature included local arterial dissection, non-target embolization causing ischemia, acute urinary retention, retrograde ejaculation, bleeding, inguinal hematoma, anemia, sepsis, urinary tract infection, dysuria, incontinence, urethral or bladder neck stricture, transient pelvic pain, and constipation.<sup>27</sup> The NICE overview also noted one case report of radiodermatitis due to exposure to radiation during the procedure.<sup>27</sup> The guidance committee highlighted the rate of urinary retention post-procedure and possible concerns regarding radiation exposure as a result of imaging requirements during the procedure.<sup>29</sup> The complexity of the arteries supplying blood to the prostate means that long periods of fluoroscopy may be needed during the procedure, potentially exposing clinicians and patients to high doses of radiation.<sup>111,112</sup> In addition, angiography used to map the blood flow to the prostate carries a risk of adverse reactions to the contrast media.<sup>13,29</sup>

The UK-ROPE registry also reported a low rate of complications in the 216 patients who underwent prostatic artery embolization.<sup>81</sup> Adverse events included one case of sepsis, one blood transfusion, four cases of arterial dissection, four groin hematomas, and two cases of embolization of non-target tissue.<sup>81</sup> The most common adverse events reported by patients post-embolization were hematuria (19%) and blood in the semen (13%).<sup>81</sup>

## Aquablation (AquaBeam)

The [CADTH Rapid Response](#) noted that the incidence of persistent adverse events in the papers reporting on the WATER trial was considerably lower with aquablation than with TURP at three, six and 12-months follow-up.<sup>16</sup> The incidence of incontinence and sexual dysfunction was similar for both

procedures at six months.<sup>16</sup> When compared with TURP, aquablation studies reported higher rates of post-operative bleeding and blood transfusion, particularly in the treatment of larger prostates.<sup>30</sup> A recent analysis of clinical trial and unpublished data suggests that bleeding in patients undergoing aquablation can be reduced by using certain procedures to achieve hemostasis.<sup>113</sup> In the 19 Canadian patients in the WATER II study none of the patients required blood transfusion – possibly due to the different post-procedure protocols used.<sup>41</sup> The Canadian study reported six adverse events that persisted at three months: five voiding problems, and one urinary tract infection.<sup>41</sup>

In the WATER II study of aquablation treatment of large prostates, adverse events that persisted at six months included urinary tract infection (5.9%), meatal stenosis or narrowing of the opening of the urethra (3%), dysuria (3%), pain, urethral stricture, urinary retention, incontinence and urgency – each of which occurred in from 1% to 2% of patients. The 2019 comparison of patients treated with aquablation in the WATER (small-to-moderate sized prostates) and WATER II (large prostates) studies, found a higher rate of complications in patients with larger prostates.<sup>98</sup> At 12-month follow-up, five patients (5%) had experienced serious adverse events.<sup>92</sup> Ten patients experienced bleeding that required blood transfusion before hospital discharge.<sup>92</sup> Three patients experienced cardiovascular events post-procedure (one stroke that lead to multisystem organ failure and two cardiac arrests). All patients recovered and whether these events were related to the aquablation procedure is unclear.<sup>67</sup> Three patients (3%) in the WATER II study experienced incontinence at 12-month follow-up.<sup>92</sup>

A 2019 Italian review of nine aquablation studies noted the following adverse events: bleeding (2% to 19% of patients), urinary retention (8%), bladder spasm (3%), urethral stricture and urinary incontinence (both occurred in less than 1% of patients), dysuria (1% to 10% of patients), and urinary tract infections (up to 18% of patients).<sup>114</sup> Other reported adverse events included pain, voiding dysfunction, and urinary retention requiring re-catheterization.<sup>114</sup>

The 2019 ECRI Institute brief on aquablation noted a US FDA recall of malfunctioning AquaBeam handpieces.<sup>31</sup> The FDA's MAUDE database includes numerous reports, mainly involving post-operative bleeding and the need for retreatment or, in some instances, blood transfusion.<sup>115</sup> Two reports of death due to cardiac arrest post-procedure were not considered related to the aquablation treatment.<sup>115</sup>

## Concurrent Developments

Several trials of these treatments are planned or still ongoing, including:

- the Rezūm XL study ([NCT03605745](#)) is further investigating the use of water vapour thermal therapy in larger prostates<sup>24,116</sup>
- the five-year continuation of the WATER randomized controlled study comparing aquablation with TURP ([NCT02505919](#), estimated study completion date February 2020)
- a randomized controlled trial comparing aquablation with holmium laser therapy and photoselective vaporization of the prostate ([NCT03846700](#), estimated study completion date December 2019)
- the OPEN WATER international post-marketing study of aquablation ([NCT02974751](#), estimated study completion date July 2020)
- the completion of the WATERII study of aquablation for larger prostates ([NCT03123250](#), estimated study completion date March 2021)
- water vapour thermal therapy, using the Poseidon System, is under investigation for the treatment of prostate cancer ([NCT04087980](#)).<sup>117,118</sup>

Many other innovations for the treatment of lower urinary tract symptoms due to BPH are also under investigation. Magnetic resonance (MRI)-guided focused laser ablation of the prostate is being trialled in the US.<sup>119</sup> Systems that use high-intensity focused ultrasound (HIFU) with real-time MRI guidance to ablate prostatic tissue are also in development. These include the Tulsa-Pro (Profound Medical Corporation) and the Sonablate (SonaCare Medical).<sup>120</sup> HistoSonics Inc. is developing a Robotically Assisted Sonic Therapy system that uses histotripsy – pulsed HIFU – to ablate tissue.<sup>120</sup>

Prostatic stents and implantable devices intended for temporary, short-term use include the Spanner (Abbey Moor Medical); Memokath (Doctors and Engineers);<sup>100</sup> UroLume Wallstent (American Medical Systems); iTIND (which is the second generation of the TIND device; Medi-Tate Ltd.), ClearRing (ProArc Medical), implantable rings that compress prostatic tissue away from the urethra; the Zenflow Spring System (Zenflow, San Francisco, CA), a nitinol spring placed into the urethra; and the Butterfly Prostatic Retraction device (Butterfly Medical Ltd.), a stent implanted into the urethra to retract the lateral lobes of the prostate.<sup>13,22,100,121,122</sup> These treatments are still in early trials or in limited use in some countries.<sup>13,100</sup> Early studies note potential complications with some of these temporary devices, including

stent migration or misplacement and infection,<sup>14</sup> possible exacerbation of lower urinary tract symptoms, and encrustation.<sup>7</sup>

Intraprostatic injections using drugs such as topsalsyn (PRX302) or botulinum neurotoxin-A are also being investigated for the treatment of lower urinary tract symptoms due to BPH.<sup>15,22</sup>

## Forthcoming Health Technology Assessments

In November 2019, NICE considered further evidence on water vapour ablation (Rezūm).<sup>46</sup> Draft guidance, including assessment of costs, is currently posted for stakeholder comments; new guidance is expected in April 2020.<sup>46</sup>

Health Quality Ontario is undertaking a comprehensive assessment of prostatic artery embolization for BPH. This assessment is expected to be published in the Fall of 2020.<sup>123</sup> In 2017, the Ludwig Boltzmann Institut, in Austria, assessed the evidence on prostatic artery embolization available at that time, noting that it was insufficient to determine whether the treatment is as effective and safer than TURP or prostatectomy.<sup>124</sup> The assessment called for a re-review of the evidence in 2021 when results from registry studies and further trials should be available.<sup>124</sup>

## Considerations for Use

### Clinical expertise and training

A 2010 study projected that, by 2018, Canada would have a shortage of urologists given the large, aging baby boom generation.<sup>4</sup> Although first-line drug treatments for BPH are typically provided by primary care physicians, the study estimated that from 2005 to 2018 the number of Canadians older than 50 who would seek treatment for BPH symptoms could increase by 41.3%, and that across the country a total of 799 urologists would be needed.<sup>4</sup> The Canadian Medical Association data indicates that, as of 2018, Canada had 716 urologists in practice.<sup>125</sup>

Prostatic artery embolization, in particular, is technically demanding and NICE guidance recommends that it should be performed by an interventional radiologist with training and experience with the procedure.<sup>29</sup> Increased clinician experience with prostatic artery embolization may also minimize the use of fluoroscopy and therefore also the radiation dose to patients and health care staff during the procedure.<sup>82</sup>

### Outpatient versus inpatient procedures

If these newer treatments can be performed as outpatient procedures, cost savings due to decreased hospitalizations

could result.<sup>26,45,54</sup> Although it is not performed as an outpatient procedure, aquablation takes less time in the operating room than TURP and could potentially reduce operating room procedural times for BPH treatments.<sup>41</sup> Prostatic artery embolization, performed in an interventional radiology suite rather than an operating room, may also reduce hospital costs.<sup>48</sup> However, some patients may still require hospitalization and general anesthesia to undergo these procedures.<sup>82</sup>

## Patients with prostate cancer

Unlike surgical procedures for BPH, these less invasive treatments do not provide a tissue sample, and an opportunity to screen for prostate cancer may be missed.<sup>47,114</sup>

A recent report of 156 patients treated with prostatic artery embolization (including patients with localized prostate cancer) at one UK centre noted that this treatment can also provide relief of lower urinary tract symptoms for prostate cancer patients — many of whom may live with localized cancer for many years.<sup>82</sup>

## Uptake

Prostatic urethral lift, water vapour thermal therapy and aquablation are not yet widely available in Canada. Two Canadian urologists are performing UroLift procedures, and one centre in Ontario is offering prostatic artery embolization. One centre, in Toronto, has the aquablation system (funded through private philanthropy) (Dr. Dean Elterman, University of Toronto, Toronto, ON: personal communication, 2019 Dec 17). Rezūm water vapour therapy is available at centres in Montreal, Toronto, and Hamilton. In future it may also be offered in Vancouver. (Dr. Larry Goldenberg, University of British Columbia, Vancouver, BC: personal communication, 2019 Dec 11).

UK specialists commenting on the NICE guidance on aquablation noted that, in 2016, three UK centres were offering aquablation.<sup>126</sup> They also noted that further uptake of this treatment would depend largely on the cost of the technology.<sup>126</sup> One specialist suggested that a small number of centres that handle a high volume of patients would be the most advantageous use of this technology.<sup>126</sup>

Studies in the US and Australia suggest that less invasive BPH treatments, such as photoselective laser vaporization and holmium laser enucleation are increasingly being used rather than TURP.<sup>8,127</sup> The Australian analysis of private hospital data found the number of TURPs performed decreased by 23% during the past 20 years, while procedures such as prostatic urethral lift made up 8% of BPH procedures in 2017.<sup>127</sup> Prostatic urethral lift was used more often in younger Australians (18.6% in those aged 45 to 54, versus 2.4% in those older than 85).<sup>127</sup> The authors

speculate that part of the reason behind the uptake of UroLift may be that the procedure does not require expensive equipment, compared with, for example, photoselective laser vaporization.<sup>127</sup> At the time of the study, prostatic artery embolization and Rezūm were just beginning to be offered in Australia.<sup>127</sup> Canada may be following these trends, but more slowly.<sup>8</sup> Which treatment options are offered to individual patients will depend on the technologies available to them locally, and on their clinician's training and expertise with a particular technology.<sup>42</sup>

The Ekobi Embolization Microspheres have been used for prostatic artery embolization or for uterine fibroid embolization procedures at three centres in Alberta (Michael W. Stewart, IMBiotechnologies Ltd., Edmonton, AB: personal communication, 2019 Oct 11). Other Canadian centres may be offering prostatic artery embolization using different embolization materials.

## Final Remarks

There is some evidence comparing these less invasive technologies with TURP, but studies are needed that directly compare them with each other, and to other less invasive treatments, such as photoselective laser vaporization. Ideally, these studies would be head-to-head, randomized controlled trials, with longer follow-up, that fully assess clinical effectiveness, costs, adverse events, durability of outcomes and retreatment rates, and patient satisfaction.<sup>30,47,48,90,128</sup>

The 2019 American Urological Association guidelines on BPH note the need for more evidence to support incorporation of these newer treatments into clinical practice.<sup>21</sup> The association outlined the following factors for successful BPH treatments from both patient and clinician perspectives:

### Patient criteria:

- tolerability of the procedure
- fast and long-lasting symptom relief
- rapid recovery
- safety
- affordability.

### Clinician criteria:

- a procedure that can be performed in an outpatient setting with minimal anesthesia
- a procedure with a short learning curve that is technically easy to perform
- evidence that is generalizable from clinical studies to broader patient groups.<sup>21</sup>

The association guidelines comment that many individuals discontinue drug therapies for BPH, yet relatively few go on to seek surgical treatment — an indication that less invasive treatment options are needed.<sup>21</sup>

If these new treatments become alternatives to first-line drug therapies, as several study authors have suggested, the patient population that is seeking and eligible for these treatments is likely to increase.<sup>25,30,72,83</sup> Specialist consultants commenting on the NICE aquablation guidance noted that TURP is the “bread and butter of urology,” and that technologies that offer patients an alternative to TURP could have a major impact in terms of the number of people seeking treatment.<sup>126</sup>

Clinical practice guidelines stress the need for shared decision-making, with patients fully informed of the shortcomings in the available evidence, including adverse events, long-term effectiveness, and the possible need for subsequent retreatment.<sup>7,11</sup>

These technologies have the potential to benefit patients through reduced adverse events and improved preservation of sexual function. They may also offer health care cost savings if they can be provided as outpatient procedures or with reduced lengths of hospital stay — but real-world evidence confirming these potential benefits is still needed.



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