REZUM—WATER VAPOR THERMAL THERAPY FOR THE TREATMENT OF BENIGN PROSTATIC HYPERPLASIA

HEALTH TECHNOLOGY ASSESSMENT REPORT

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All inferences, opinions, and conclusions drawn in this publication are those of the authors and do not necessarily reflect the opinions or policies of the British Columbia Ministry of Health, or any individual stakeholders involved in this project.

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List of Abbreviations

AEEP	Anatomic Endoscopic Enucleation of the Prostate
BC	British Columbia
BIA	Budget Impact Analysis
BIM	Budget Impact Model
BPH	Benign Prostate Hyperplasia
CADTH	Canadian Agency for Drugs and Technologies in Health
CDSR	Cochrane Database of Systematic Reviews
CEA	Cost-Effectiveness Analysis
CEAC	Cost-Effectiveness Acceptability Curve
CENTRAL	Cochrane Central Register of Controlled Trials
CI	Confidence Interval
CIHI	Canadian Institute for Health Information
CONSORT	Consolidated Standards of Reporting Trials
CPI	Consumer Price Index
CUA	Canadian Urological Association
CV	Coefficient of Variance
DAD	Discharge Abstract Database
DARE	Database of Abstracts of Reviews of Effects
EPHPP	Effective Public Health Practice Project
EQ5D	EuroQol Five-dimension Scale Questionnaire
EQ-5D-3L	EuroQol-5 dimensions–3 levels
FHA	Fraser Health Authority
FNHA	First Nation Health Authority
FTE	Full-Time Equivalent
GP	General Practitioners or Family Physicians
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HCC	Health Care Costs
HoLEP	Holmium Laser Enucleation of the Prostate
HTA	Health Technology Assessment
HTAO	Health Technology Assessment Office
ICD	International Classification of Diseases
ICER	Incremental Cost-Effectiveness Ratio
ICUR	Incremental Cost-utility Ratio
IPSS	International Prostate Symptom Score

LOCF	Last Observation Carried Forward
LUTS	Lower Urinary Tract Symptoms
LY	Life-Years
MA	Meta-Analysis
MD	Mean Difference
MeSH	Medical Subject Heading
MOH	Ministry of Health
MSP	Medical Services Plan
NA	not available
NA	Not Available/Not Reported
NHA	Northern Health Authority
NICE	National Institute for Health and Care Excellence
NMA	Network Meta-Analysis
NR	not reported
OR	Odds Ratio
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSA	Prostate Specific Antigen
QA	quality assessment
QALY	Quality-Adjusted Life-year
QoL	Quality of Life
RCT	Randomized Controlled Trials
RoB	Risk of Bias
RR	Relative Risk
Rx	Medical Prescription / Pharmacotherapy
SD	Standard Deviation
SR	Systematic Review
TUIP	Transurethral Incision of the Prostate
TURP	Transurethral Resection of the Prostate
USD	U.S. Dollars
VCH	Vancouver Coastal Health Authority
WVTT	Water Vapor Thermal Therapy

Executive Summary

Benign prostatic hyperplasia (BPH) is an enlargement of the prostate gland and is a common condition among men aged 60 years and older. Approximately 38% of men aged 80 years and older have BPH. Symptoms of BPH include frequent urination and urine retention. For some men, BPH can significantly impact quality of life. The majority of men with mild to moderate symptoms are treated with medications.

For men who have moderate to severe symptoms or for men for whom medication did not relieve their symptoms, transurethral resection of the prostate (TURP) may be recommended. TURP is a minimally invasive surgery performed in a hospital setting. Although TURP is an effective treatment for BPH, the procedure can damage other tissues and cause erectile dysfunction.

Rezum is a new technology which uses steam to ablate benign prostate tissue via a cystoscope. The procedure may cause less injury to other tissues and therefore potentially reduces the risk for sexual dysfunction. Rezum is a minimally invasive procedure which can be performed in a non-hospital setting and is gaining support amongst clinicians.

A systematic review to determine the effectiveness of Rezum did not identify any studies directly comparing Rezum with TURP. We identified one network meta-analysis that concluded that TURP is more effective than Rezum and two other network meta-analyses found no significant difference on key outcome measures between the two procedures. At this time, the evidence base in support of Rezum is lacking. High quality studies directly comparing Rezum with TURP are required.

Chapter 1 Background and Problem

1.1 Purpose of this health technology assessment (HTA)

The objective of this health technology assessment is to determine the clinical effectiveness, and if appropriate, the cost-effectiveness and budget impact of Rezum water vapor thermal therapy compared with transurethral resection of the prostate (TURP) for patients with benign prostatic hyperplasia (BPH) in British Columbia (BC).

1.2 Primary policy questions

1. What is the clinical and cost-effectiveness of Rezum in the treatment of patients with BPH in BC?
2. What is the budget impact of introducing Rezum across BC in the treatment of patients with BPH?

1.3 Natural history of benign prostate hyperplasia

The prostate gland is a male pelvic organ. It is located between the bladder and rectum and surrounds the proximal urethra. BPH occurs when the prostate gland develops nodules that result in the enlargement of the gland.[1] It is referred to as benign because of the non-cancerous nature of the disease. Because of its location, an enlarged prostate gland will limit the flow of urine through the proximal urethra and will also affect the ability of the bladder to store urine. BPH commonly occurs in men over 40 and is most prevalent among elderly men. Research suggests that age, diabetes, and obesity are risk factors for developing BPH.[2-4] Lower urinary tract symptoms (LUTS) can be the result of BPH.[1] LUTS include difficulty urinating, urine retention, frequent urination, nocturia, incomplete urination, and having a weak urinary stream.[1, 3] Although rare, complications of BPH include urinary stones, urinary tract infections,

and renal insufficiency. A combination of clinical examination (e.g., symptom history, digital rectal exam) and laboratory tests (e.g., urinalysis, Prostate Specific Antigen (PSA) test) are used to diagnose BPH.[5, 6] Imaging technology, such as ultrasound, can also be utilize to assess the prostate volume. The severity of LUTS can be assessed using the International Prostate Symptom Score (IPSS). An IPSS score of ≥8 indicates moderate to severe LUTS.[7]

1.3.1 Condition severity

1.3.1.1 How does the condition affect a patient's quality of life?

BPH is associated with decreased quality of life and the magnitude of the decrease is dependent on symptom severity.[8] The EQ-5D utility score for mild, moderate, and severe LUTS due to BPH is 0.9, 0.81, and 0.73 respectively.[8] Patients' lifestyle may also be significantly impacted by frequent urination and episodes of incontinence. The impact of BPH symptoms, which can significantly impact a patient's life, may not be adequately captured by generic quality of life tools.

1.3.1.2 How does the condition affect a patient's expected life?

BPH is not associated with decreased life expectancy and is not a risk factor for prostate cancer.[9]

1.3.1.3 How does the condition affect the caregiver to the patient?

Frequent urination and episodes of incontinence may prevent patients from participating in some family and social activities which may have an impact on family and social life. Frequent night time urination by the patient might affect the sleep quality of the bed partner. Frequent night time urination may lead to higher risk of fall which could cause disability. However, the pathophysiology of BPH is not associated with increased risk for disability.

1.3.2 Condition prevalence

1.3.2.1 How many people live with this condition in BC?

A systematic review estimated that the pooled prevalence of BPH among men aged ≥40 years was 26.2% (95% CI: 22.8–29.6%).[3] The prevalence of BPH increases with age. Among men aged 40-49 years an estimated 14.8% of men have BPH and this increases to 38.4% among men ≥80 years.[3] Using 26.2% as a point estimate, there are approximately 353,700 men age 40 and older in BC who have BPH. BPH is often underdiagnosed and undertreated. [10] A European study demonstrated that approximately 19% of men with LUTS sought medical care; and approximately 11% received treatments.[10] The BC administrative data was queried for the years 2020-2021 using ICD-9 code 600 ("hypertrophy (benign) of prostate without urinary obstruction and other lower urinary tract symptoms (LUTS)") and the names of common medications used for the treatment of BPH. The query identified [redacted] in BC with diagnosis of BPH.[11]

1.3.2.2 What is the public health impact in BC? Might other populations be affected indirectly either positively or negatively? What population(s) are these?

BPH is not a communicable disease, and may impair social functioning but is unlikely to lead to disability. BPH is unlikely to affect other members of the population. However, patients suffering from severe symptoms of LUTS related to BPH or complications from the surgical interventions for BPH (e.g., blood in urine), will utilize the health care system, such as the emergency room.

1.4 Treatment options

The Canadian Urological Association (CUA) 2018 guideline provides treatment recommendations for BPH. The CUA guideline suggests that therapeutic decision-making should be guided by symptom severity, degree of bother, and patient preference.[6] Patients

with mild symptoms are recommended to make lifestyle changes and follow up by physicians periodically. Lifestyle changes include:

- Fluid restriction, particularly before bedtime
- Avoidance of caffeinated beverages, alcohol, and spicy foods
- Avoidance/monitoring of some drugs (e.g., diuretics, decongestants, antihistamines, antidepressants)
- Timed or organized voiding (bladder retraining)
- Pelvic floor exercises
- Avoidance or treatment of constipation

The CUA guideline recommends additional treatments for patients with moderate to severe BPH with bothersome symptoms. These treatment options can be divided into two main categories-- pharmacological treatments and surgical treatments. The primary therapeutic goals of BPH treatment are symptom relief and the reduction of prostate volume.

1.4.1 Pharmacological treatments

1.4.1.1 Description

Most patients with BPH are managed with pharmacological treatments. There are several classes of medications that are commonly used in BPH. The 2018 CUA guideline suggests first-line treatment for LUTS related to BPH using alpha-blockers and 5-alpha-reductase inhibitors (5ARIs). Alpha-blockers are effective for reducing LUTS but they do not reduce the prostate volume or the need of BPH-related surgery.[6] 5ARIs are effective for reducing the prostate volume, the risk of acute urinary retention, and the need of BPH-related surgery in patients with prostate volume greater than 30 cc.[6] The 2018 CUA guideline also

recommends using a combination of both alpha-blocker and 5ARIs to treat patients with a prostate volume > 30 cc. Alpha blockers can be discontinued from the combination if the patient's symptoms improve.

Nocturnal polyuria can be a bothersome symptom of BPH. The CUA guidelines recommend using desmopressin for the treatment of nocturnal polyuria.[5, 6] Second-line treatment options include antimuscarinics, beta-3 agonists, and phosphodiesterase type 5 inhibitors. However, the quality of evidence supporting their use is low and the guideline suggests only trying these medications after discussing the risks and benefits with the patient.

Common adverse effects of pharmacotherapy include sexual dysfunction, orthostatic hypotension, and dizziness. Some of the adverse effects may lead to falls which may have serious consequences among older adults (e.g., fracture).

1.4.1.2 Current usage in BC

The BC administrative data was queried for the years 2020-2021 using ICD-9 code 600 ("hypertrophy (benign) of prostate without urinary obstruction and other lower urinary tract symptoms (LUTS)") and the names of common medications used for the treatment of BPH (as described in the CUA guideline). The query identified [redacted] men in BC with diagnosis of BPH of whom approximately 54% received pharmacological treatment in 2020-2021. The BC public payer spent [redacted] in 2020-2021 for BPH-related MSP claims and medication costs.

1.4.2 Surgery

1.4.2.1 Description

The surgical treatment of BPH can be divided into two main types, open surgery and minimally invasive surgery. There are several different types of minimally invasive procedures that can be used to treat BPH. The criteria to determine which one is suitable depends on the

patients' profile. The most common type of minimally invasive surgery is transurethral resection of the prostate (TURP). TURP, either monopolar or bipolar, is recommended by CUA for patients with prostate volume between 30 cc to 80 cc. If the prostate volume is less than 30 cc, transurethral incision of the prostate (TUIP) is recommended by CUA. In the case when prostate volume is greater than 80 cc, open surgery is recommended. Anatomic endoscopic enucleation of the prostate (AEEP) is added as recommended surgical procedure for prostate volume greater than 30 cc in the 2022 update of CUA guideline.[5] For elderly patients with significant comorbidities or greater anesthesia risks, transurethral microwave therapy is recommended by CUA. All the surgical procedures share a common goal to reduce the size of the prostate and improve LUTS.

Patients undergoing TURP require a general or spinal anesthesia. TURP is carried out using a resectoscope, which is a thin metal tube containing a light, camera and loop of wire. This is passed along the urethra to reach the prostate. The loop of wire is then heated with an electric current and used to remove the section of the prostate. A catheter is then inserted into the urethra to pump fluid and flush away pieces of prostate that have just been resected. Patients may stay in the hospital for one or two days after the procedure.[12]

1.4.2.2 Current usage in BC

According to a recent U.S. study, the incidence of BPH-related surgery was approximately 2% per year for the first five years of diagnosis and approximately half of the surgical procedures are TURP.[13] From the BC administrative data, there were [redacted] patients with BPH diagnosis code who had the fee code 08311 in 2020-2021.[11] The fee code 08311 was the fee code in MSC fee schedule that described as prostatectomy with

transurethral approach.[14] Limitation of using this fee code was that it was not limited to TURP alone. As the result, the number of patients who received TURP could be overestimated. This approach could be used as references to estimate how many patients received TURP each year which was close to the estimate from the U.S. study.[13]

1.4.3 Rezum

1.4.3.1 Description

The Rezum water vapor thermal system is manufactured by NXThera/Boston Scientific (Marlborough, MA) and obtained regulatory approval from Health Canada in 2018.[15] The Rezum system uses convective energy in the form of steam to ablate benign prostate tissue. The steam is applied through a single-use transurethral handpiece (cystoscope) using a retractable needle. The steam cannot cross physical boundaries therefore will travel only within the target prostate compartments.[16] The outpatient procedure uses 9 second steam injections that reduce prostate size with low risk of injury to adjacent structures thereby potentially reducing the risk of sexual dysfunction. The average procedure time is 8 minutes for Rezum as compared with 60 to 90 minutes for TURP.[17] Rezum is a minimally invasive procedure which could be performed as an outpatient in a non-hospital medical setting or surgical facility.

Potential advantages of Rezum might also include that it is an outpatient procedure that does not require hospital stay. For older adults, avoiding an overnight hospital stay may also reduce the risk of contracting a hospital-acquired illness.

1.4.3.2 Current usage in BC

Rezum is currently not publicly funded in BC. Four urologists practicing in BC were interviewed of whom one uses Rezum in private practice (please see Chapter 3 for additional details). Rezum is presumed to cause fewer adverse events compared to TURP, such as erectile

dysfunction.[17] While not intended to replace TURP, Rezum can be an alternative to TURP in the care pathway providing additional treatment options.

1.5 Research questions

1) What is the current standard of care for patients with BPH in BC (e.g., status quo clinical care pathway)?
    i) How is Rezum incorporated into the current standard of care (e.g., intervention (Rezum) clinical care pathway)
2) What are the guidelines in BC for the treatment of BPH?
3) Which provinces and territories currently use Rezum and how is Rezum funded?
4) Have other jurisdictions undertaken an HTA of Rezum to treat patients with BPH?
    i) If so, what were their findings?
5) What are patient perspectives and experiences with Rezum in BC?
6) What is the stakeholder/clinician perspectives and experiences with Rezum in BC?
7) What is the comparative clinical effectiveness of Rezum compared with TURP?
8) What is the cost-effectiveness of Rezum compared with TURP?

Chapter 2 Jurisdictional Scan

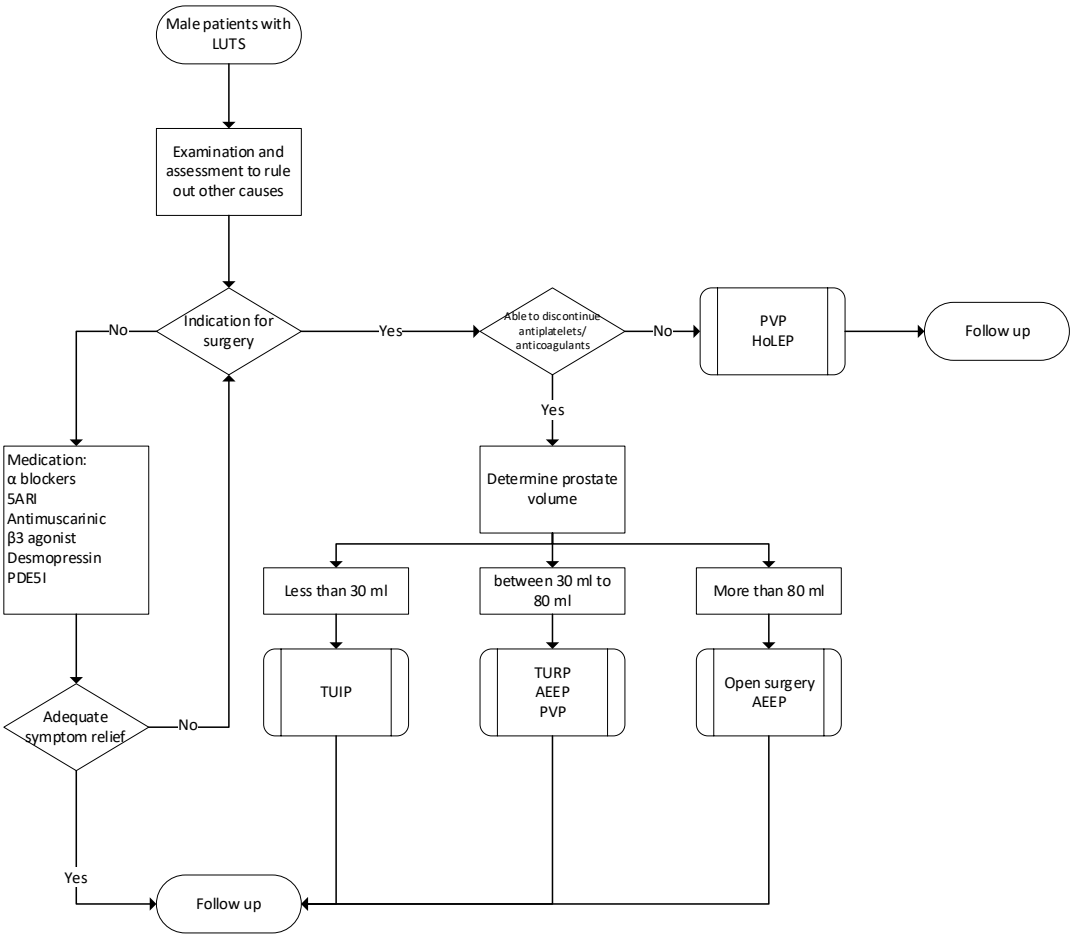
2.1 Care Pathway

The care pathway was inspired by the 2018 CUA guideline and the 2022 update of the guideline.[5, 6] In summary, patients with LUTS are assessed for the cause. If BPH is determined to be the cause of LUTS, patients are advised to try medications first. In the case when medications fail to achieve the treatment goal or if patients prefer surgery, patients are assessed for eligibility for surgery. The CUA criteria for surgery include:

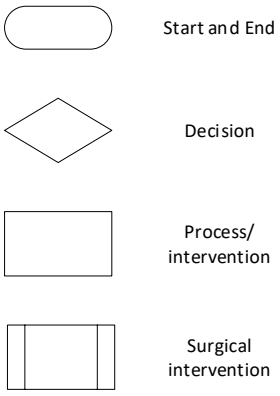
- recurrent or refractory urinary retention;
- recurrent urinary tract infections (UTIs);
- bladder stones;
- recurrent hematuria;
- renal dysfunction secondary to BPH;
- symptom deterioration despite medical therapy; and
- patient preference.

If surgery is chosen, CUA suggests follow-up with patients to assess treatment success in four to six weeks after catheter removal. The length of follow-up will depend on the intervention and the condition of the patient.

Figure 2.1. Care pathway of BPH.



Note:
5ARI = 5-alpha-reductase inhibitors
AEEP = anatomic endoscopic enucleation of the prostate
LUTS = Lower urinary tract symptom
PDE5I = Phosphodiesterase type 5 inhibitors
PVP = Photoselective vaporization of the prostate
TUIP = Transurethral incision of the prostate
TURP = Transurethral resection of the prostate



2.2 Guidelines for the treatment of BPH

	CUA	AUA	EAU

1st line medications	5ARI Alpha blockers	5ARI Alpha blockers	5ARI Alpha blockers
2nd line medications	Phosphodiesterase Type 5 Inhibitors Beta-3 agonist Antimuscarinic	Phosphodiesterase Type 5 Inhibitors Beta-3 agonist Antimuscarinic	Phosphodiesterase Type 5 Inhibitors Beta-3 agonist Antimuscarinic
Surgical options for prostate volume 30 to 80 cc	TURP AEEP PVP Rezum as possible alternative	TURP TUVP PVP Laser Enucleation Rezum as possible alternative	TURP PVP No recommendation issue for Rezum

Note: 5ARI = 5-alpha reductase inhibitors; AEEP = Anatomical endoscopic enucleation of the prostate; HoLEP = PVP = Photo-Vaporization of the Prostate; TURP = Transurethral Resection of the Prostate; TUVP = Transurethral Vaporization of the Prostate.

BC Guidelines, developed by the Guidelines and Protocols Advisory Committee (an advisory committee to the Medical Services Commission), has not published a BPH guideline.[18]

The CUA published a guideline for the diagnosis and management of BPH in 2018 and an update of the guideline was published in 2022.[5, 6] The details regarding the therapy recommendations have been described in section 1.4. In summary, CUA recommends medications as the first-line therapy for BPH. For a selected subgroup of patients who are eligible for surgery, CUA recommends TURP for patients with prostate volume between 30 cc to 80 cc, which is also the same target population of Rezum. The CUA guideline suggests that Rezum can be an alternative to TURP.

The American Urological Association (AUA) published a guideline for the management of BPH in 2021 which recommends the same treatment as CUA.[19, 20] The AUA guideline also suggests that Rezum can be considered as an alternative to surgical treatment for prostate volume between 30 cc to 80 cc. But the suggestion is based on low level of evidence.

The European Association of Urology published a guideline for BPH.[21] It provides the same recommendations regarding medication, TURP, TUIP, and open surgery as the CUA

guideline. The EAU guideline summarizes the evidence for Rezum but does not make any recommendations regarding deployment of Rezum.

2.3 HTA jurisdictional scan

2.3.1 Methods

HTA reports were searched on relevant databases in Canada [e.g., Canadian Agency for Drugs and Technologies in Health (CADTH) (national), Health Quality Ontario (HQO) (Ontario), Institute of Health Economics (IHE) (Alberta), Institut national d'excellence en santé et en services sociaux (INESSS) (Quebec)] and internationally [e.g., the International Network of Agencies for Health Technology (INAHTA), TRIP, the UK's National Institute for Health and Care Excellence (NICE), Scotland, and Australia]. The following keywords were used: "rezum" and "water vapor". No restriction on intervention since there are multiple interventions included in this project.

2.3.2 Results

In total, two HTA reports were identified from the NICE and CADTH databases.

2.3.2.1 CADTH[22]

CADTH published a report in 2019 examining the clinical effectiveness of multiple minimally invasive procedures compared with an active intervention (e.g., TURP or open surgery). In their report, CADTH did not find any randomized or non-randomized study comparing Rezum with active intervention.

2.3.2.2 NICE[23]

A NICE guidance (Medical technologies guidance [MTG49]) was published in 2020, where NICE conducted an external assessment of the company's submission for adoption of Rezum in UK's National Health Service.

The evidence submitted compared Rezum to monopolar or bipolar TURP, Holmium laser enucleation of the prostate (HoLEP), GreenLight laser, open prostatectomy, and UroLift. The clinical review conducted by the manufacturer did not identify any studies comparing Rezum to any of the active interventions. The main source of the clinical evidence included one RCT comparing Rezum to sham control (Rezum II: NCT01912339) and three case series.[24-27] NICE concluded that there was strong evidence of benefit for Rezum when compared with sham, although it was noted that there is an important gap in the evidence, as no direct evidence comparing Rezum with other interventions was available.

The company's submission also included a *de novo* cost-consequence analysis using a cohort Markov modelling approach. In the economic analysis, Rezum was compared with TURP, UroLift, GreenLight laser and HoLEP over a 4-year time horizon. The main assumption of the model was that all technologies under evaluation were *equally* effective. This assumption was noted as the main limitation of the model by the NICE external review committee. The study does report that Rezum was cost saving when compared with all active comparators but the review committee noted that the model had key uncertainties associated with the inputs used due to lack of empirical evidence. In short, these findings are not relevant to our context due to the assumptions in the model and lack of relevant underlying evidence.

2.4 Provincial and Territorial jurisdictional scan

2.4.1 Methods

The BC Ministry of Health, using the intergovernmental relations network, contacted other provincial Ministries of Health with a standardized email questionnaire. If the email recipient felt that they did not have the necessary expertise to respond, they were asked to

forward the request to a knowledgeable colleague. A snowball sampling scheme was used to refer the team to any other stakeholders other than those previously recommended.

The standardized email requested a response to the following questions:

1. Is Rezum available as a treatment option for patients diagnosed with benign prostatic hyperplasia?
2. If yes:
    a. How is Rezum funded (e.g., public, private)
    b. What are the patient eligibility criteria for Rezum?

2.4.2 Results

2.4.2.1 Implementation considerations: Infrastructure: What approaches to implementation have other jurisdictions used, if applicable?

All findings are only representative of the respondent provinces at the time that the request was made. It should be noted that services may have changed by the time of the publication of this report.

Email responses were received from [redacted].

2.4.3 Conclusion

2.4.3.1 Have other jurisdictions implemented this technology?

Rezum is not publicly funded in any of the jurisdictions which responded to this request for information. There appear to be a small number of private clinics in both Ontario and Quebec where the procedure is offered; patients are responsible for paying 100% of costs.

Chapter 3 BC context and other stakeholder perspectives

3.1 Objective

To understand the experience of key clinical stakeholders in BC with treatments for benign prostatic hyperplasia, or BPH.

3.2 Methods

Prospective interviewees were sampled from a list provided by Cambie Surgery Centre in Vancouver. Each was emailed an invitation to participate, and a date and time arranged. Interviews were conducted by telephone or by Zoom, and lasted approximately 15-20 minutes each. Detailed notes were taken of each interview, and notes analyzed by one member of the C2E2 team to identify key themes. Responses were reviewed in order to determine where they spoke to specific assessment questions identified by sub-headings in the sections which follow. In the following, comments attributable to the participants are indicated by P1-P4.

3.3 Findings

3.3.1 Description of stakeholders

Five clinicians were invited to give their perspectives on the Rezum technology as part of this project, one from each of the 5 regional health authorities. Four of the contacts agreed to participate and one declined. All respondents are practicing urologists with between 2-25 years of experience, and have both hospital affiliations as well as private clinics. BHP -- benign prostatic hyperplasia -- cases are frequently seen, ranging from about 30-50% of total patient caseload across each of the four practices. Three out of four respondents have both training and practice in delivering Rezum, gained both in Canada (Ontario) and the US (Minnesota) being mentioned. (Since the interviewees are not a representative sample of BC urologists, it cannot be presumed that these are the only or the most common means by which skill

development currently occurs.) In short, these surgeons are well informed about current state of practice and recent developments in this field and well able to contribute their perspectives on the topic.

Topics addressed by the interviews included surgeons' perspectives about emerging technologies for treatment of BHP, particularly Rezum; about the patient populations for which the technology would be appropriate; knowledge of outcomes and patient satisfaction; and about factors which would likely facilitate or hinder the future uptake of Rezum in BC.

3.3.2 Overall Results

There was consensus among respondents that current standard of practice for BPH, supporting by existing guidelines (P1), was to begin with lifestyle changes and medical management of patients (e.g., with alpha blockers) (P1, P3). This can go on for many years (P4). More complex cases, e.g., where kidney stones or renal disease are involved, go directly to TURP (P3). TURP, in particular green light laser, is also the standard follow-up therapy where medical management fails to relieve systems (P1, P3)

Participants also agreed that Rezum was one of a number of emerging or horizon technologies in this field. Specifically mentioned were (a) UroLift (a type of staple which pulls the tissues of an enlarged prostate to the side in order to increase the opening for a blocked urethra[a]), and (b) iTIND (a device implanted for 5-7 days which widens the urethral opening)[b]. There are other emerging technologies as well, which were not explicitly noted during the interviews – for instance, prostatic arterial embolization, robotic waterjet and transurethral

[a] https://www.urolift.com/what-is-urolift
[b] https://www.itind.com/

microwave (TUMT), as well as pharmacological options such as the tadalafil/finasteride combination. Among the options discussed by the stakeholders, Rezum appeared to be the "winner" (P2, P4) as it is "gaining some traction in other settings" (P3). One advantage is that the other technologies make it more difficult to subsequently provide laser treatment (P4). Three of the four interviews had some direct experience in delivering Rezum, either as part of recent clinical trials or in residency training outside of British Columbia (in Toronto or Minnesota). Only one is currently delivering the procedure in their private practice, with an average of about one case/week.

While recognizing that the clinical literature is still relatively limited, these respondents believed that the evidence show Rezum to be safe (P1) and to result in positive patient outcomes, such as improved voiding (P1) and few side-effects or post-procedure complications (P2). Patient satisfaction is thought to be high, with quality of life improvements (P1).

P1 suggested that surgeons should "pick patients carefully" for this procedure. The appropriate patient population was identified in these physicians' opinion as younger patients, e.g., 40-60 years of age (P2, P4), for whom maintaining sexual function, ejaculation and orgasm is an important quality of life consideration (P2, P3, P4), or who wish an alternative to long-term on-going medication use (P4). Prostates should be smaller than 80 grams (P1, P2). According to P4, these considerations mean that Rezum is "likely only for a minority of patients," perhaps 10% of those with BHP as a rough estimate.

Respondents were aware of only one practice in BC where the procedure was offered; they did perceive it was more commonly available privately in Ontario (P1, P2) and Quebec (P4), as well as in the United States (P3) and in Europe (P4). Physicians felt that there would be

some interest among BC physicians in providing this procedure, given that it was relatively simple to learn to deliver, could be done quickly under local anesthetic in the clinic setting, and that "patients were asking for it". Uptake would of course be greater if the procedure were to be publicly funded, which reduces the economic barriers (P4).

Overall however, while one respondent felt that the procedure was "likely what we are going to in the future" (P3), the others expected more limited uptake in the near term. "I don't think it will replace all the other options" (P2). P1 noted that the future was uncertain and that given rapid evolution of new techniques and approaches, that Rezum too might be superseded by other developments before too long (P1). It may turn out to be an "in-between" treatment, which reduces use of medicines and postpones other surgery for a time (P4). In other words, Rezum probably should not be conceived as an either/or treatment, but as a both/and option to be delivered in combination with other care options over time as clinically appropriate for individual patients. This could be valuable as the respondents perceive that there can be lengthy waits for TURP surgery, particularly in rural areas (P1, P3).

3.3.3 Population, cultural and socioeconomic impacts

3.3.3.1 To what degree does the intervention improve a patient's family/community?

Like current treatments, symptom relief would improve quality of life. Compared to TURP, Rezum's limited impact on sexual functioning would be considered to improve quality of life for patients and partners where this is a priority.

3.3.3.2 Does this technology alleviate or exacerbate inequities that already exist for different patient populations accessing care?

This was not directly addressed by respondents. However, since Rezum is only available currently by private-pay, access is likely most available to those of higher socio-

economic status. That being said, persons of more limited means or lower socioeconomic status may well be unable to take time off work, or at threat of losing their position due to poor performance related to disrupted sleep after often waking at night-time to urinate. They may feel compelled to pay for private procedures, despite the financial challenges, because they may believe that they cannot afford not to. In other words, the current availability of the technology, to the extent that it is effective, may contribute to inequities in care.

3.3.4 Patient experience and autonomy

3.3.4.1 Does the intervention improve how a patient is treated (respect, dignity, choice of treatment) vs. the comparator?

Based on their awareness of the limited clinical literature, and to some extent their own experiences, stakeholders believe that Rezum patients are satisfied with the procedure and outcomes are perceived to be at least comparable to standard care. Patients who choose to access the treatment are perceived to be highly informed and motivated, to the extent of traveling out of province to seek out this care. For patients whose priority is maintaining sexual function, Rezum is a particularly attractive option.

3.3.5 Environmental considerations

Environmental issues were not directly addressed by the stakeholders. Given however that Rezum can be delivered in physicians' clinics, and TURP is performed in an operating room and may involve an overnight stay, we can presume that Rezum consumes fewer resources and has a lesser environmental impact in that regard.

3.3.6 Implementation considerations and operational challenges

3.3.6.1 Status quo: How is the technology currently provided? How is it funded? What human resources are currently required for the procedure (e.g., admin staff, nurses, etc.)? What are the infrastructure requirements for the procedure (e.g., equipment,

OR time, etc)? What are the current challenges? What is currently working well? What MSP fee codes are currently being used?

Currently delivered in BC in one physician's private practice; no public funding or MSP fee codes. P3 estimates that a provider could likely deliver 2 procedures/hour.

3.3.6.2 Human resources: How would the capacity of service providers be impacted (i.e., Is the relevant expertise available or will clinicians require training)? What human resource recruitment and training would be required?

Rezum is perceived to be relatively easy to learn and deliver, and could even be done by junior residents under supervision (P2). This suggests –though not explicitly stated by interviewees – that general practitioners or other non-urology specialists might also be readily trained in this procedure. As another option, the procedure might be done by urologists on short-term visits to communities without this service. Given that there appear to be minimal other resources needed in comparison to TURP (i.e., anesthetist, hospital stay, nursing and wound care, catheter care, etc.), these are prospective additional routes to scale up delivery of the procedure if deemed desirable.

3.3.6.3 Stakeholders: Are there risks (e.g. interest in or against the intervention by stakeholders, vested/financial interests of stakeholders, etc.) associated with key stakeholders (clinicians, nurses, admin, patients, caregivers, etc.) for the adoption or disinvestment of this intervention into routine care?

Public funding would increase demand. Impact on physicians would depend upon whether public reimbursement matched the amount which is currently retained by the providers from private sources of payment. If the procedure displaced surgical treatment or medication use, reduction in these costs would be appealing to current funders.

3.3.6.4 Infrastructure: What are the infrastructure requirements for the potential implementation scenario(s) (e.g., specific setting (clinics, churches, minimally invasive procedure rooms, etc) or special equipment)?

Rezum is a procedure which can be delivered under local anesthetic in physician

offices.

3.3.6.5 Other: What monitoring is in place? What, if any, changes would be necessary to ensure monitoring for this intervention?

Presumably patient outcomes would be monitored by providers in the same way as they do with current practice.

3.3.7 Ethical considerations

Ethical considerations are outside of the scope of work approved by HTAC for this HTA. An ethicist working with the HTAO/HTAC may have provided a separate analysis.

3.4 Conclusions

Albeit small, the sample of informants is highly knowledgeable and they practice in settings across the province, not only in the lower Mainland but in more remote cities as well. These clinicians believe that Rezum could be a viable treatment option for a subset of BPH patients. Despite limited length of study, they believe it to be generally safe and effective. Its advantages, particularly ease of delivery, may make it attractive to physicians but there is unlikely to be large-scale uptake without public funding, as the costs can be substantial for patients to bear directly.

Chapter 4 Patient Experience

4.1 Objective

The objective is to gain an understanding of the outcomes important to patients, in order to guide the evaluation of the clinical literature and health policy. Given the very limited extent to which Rezum is presently available, C2E2 and the HTAO collaboratively determined not to conduct a patient experience assessment for this report.

Chapter 5 Assessment of Evidence

5.1 Objectives

Clinical review

To evaluate the clinical effectiveness of Rezum when compared with TURP.

Economic review

To summarize previously published evidence on the cost-effectiveness of Rezum when compared with TURP.

5.2 Methods

5.2.1 Inclusion criteria

Table 5.1 PICO inclusion criteria

Population	Adults with benign prostatic hyperplasia for whom conservative management has failed.
Intervention	Minimally invasive water vapor thermal therapy (Rezum)
Comparator	Transurethral resection of the prostate (TURP)
Outcomes	lower urinary tract symptoms (e.g., IPSS), quality-of-life (e.g., question at the end of IPSS), Cost-effectiveness outcomes: cost, ICER, ICUR

Note: ICER = Incremental cost-effectiveness ratio; ICUR = Incremental cost-utility ratio; IPSS = International Prostate Symptom Score; TURP = transurethral resection of the prostate.

Study design

The available evidence from the CADTH and NICE reports were used as a guide for the decision to update the review, as well as a cross-reference. The primary sources of data for this review were RCTs. If the amount of evidence was deemed insufficient at the RCT level, nonrandomized studies were searched. Lower levels of evidence, such as single-arm studies, were considered hypothesis-generating and determined to be insufficient for policy decision-making.

In the absence of direct comparison study between Rezum and TURP, indirect comparison, such as network meta-analysis (NMA), was included as alternative for clinical

effectiveness.

In the economic review, only studies that conducted a full economic evaluation were included; this refers to studies that conducted a comparative analysis of the differences in both costs and benefits across treatment groups.

5.2.2 Exclusion criteria

- Non-English-language publications
- Abstract/conference proceedings
- Letters and commentaries
- Studies without an appropriate comparator arm

5.2.3 Literature search overview

An experienced medical information specialist developed and tested the search strategies through an iterative process in consultation with the review team.

Using the multifile option and deduplication tool available on the OVID platform, we searched Ovid MEDLINE® ALL, Embase, and the following EBM Reviews databases: Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, Health Technology Assessment, and NHS Economic Evaluation Database. We performed the clinical search without any filters and applied economic and health utility filters to the economic search. All searches were performed on 17 Feb 2022.

The strategies utilized a combination of controlled vocabulary (e.g., “Prostatic Hyperplasia”, “Lower Urinary Tract Symptoms”, “Steam”) and keywords (e.g., “BPH”, “LUTS”, “water vapor ablation”). Vocabulary and syntax were adjusted across the databases. No language or date limits were applied but animal-only records were removed where possible.

Results were downloaded and deduplicated using EndNote version 9.3.3 (Clarivate Analytics) and uploaded to Microsoft Excel for screening. See Appendix B for the search strategies.

5.2.4 Study selection

One reviewer screened titles and abstracts and then full texts according to the inclusion and exclusion criteria set in the PICOS question. The study flow was summarized using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram.[28]

One reviewer extracted all the data for clinical outcomes, while a second reviewer extracted all the data from economic analyses. Data were cross-checked for errors by the two reviewers. Any discrepancy was resolved by discussion when needed.

5.2.5 Quality assessment

When critical appraisal is needed, one reviewer assessed the quality of the included RCT using the Cochrane Collaboration risk of bias tool.[29] The International Society for Pharmacoeconomics and Outcomes Research Consolidated Health Economic Evaluation Reporting Standards (CHEERS)[30] was applied to assess the quality of reporting among all included comparative economic studies.

5.2.6 Data synthesis

For the clinical review, when appropriate, dichotomous outcomes were analyzed by using risk ratio (RR) or odds ratio (OR). When we found a statistically significant RR or OR we also calculated the risk difference (RD) and number needed to treat (NNT) for the outcome when possible. Continuous outcome was analyzed using weighted mean difference (WMD). If meta-analysis was not possible, the clinical data were summarized.The following data were extracted from economic studies when appropriate: country of origin, study type, model type, reported outcomes, source of funding, currency, time horizon, discount rate, interventions,

costs, quality-adjusted life-years (QALYs), incremental effects, incremental cost-effectiveness ratio (ICERs), incremental cost-utility ratio (ICUR), main assumptions, perspective, and cost and resource utilization and modelling of effectiveness. Data were qualitatively summarized.

5.2.7 Subgroup analysis

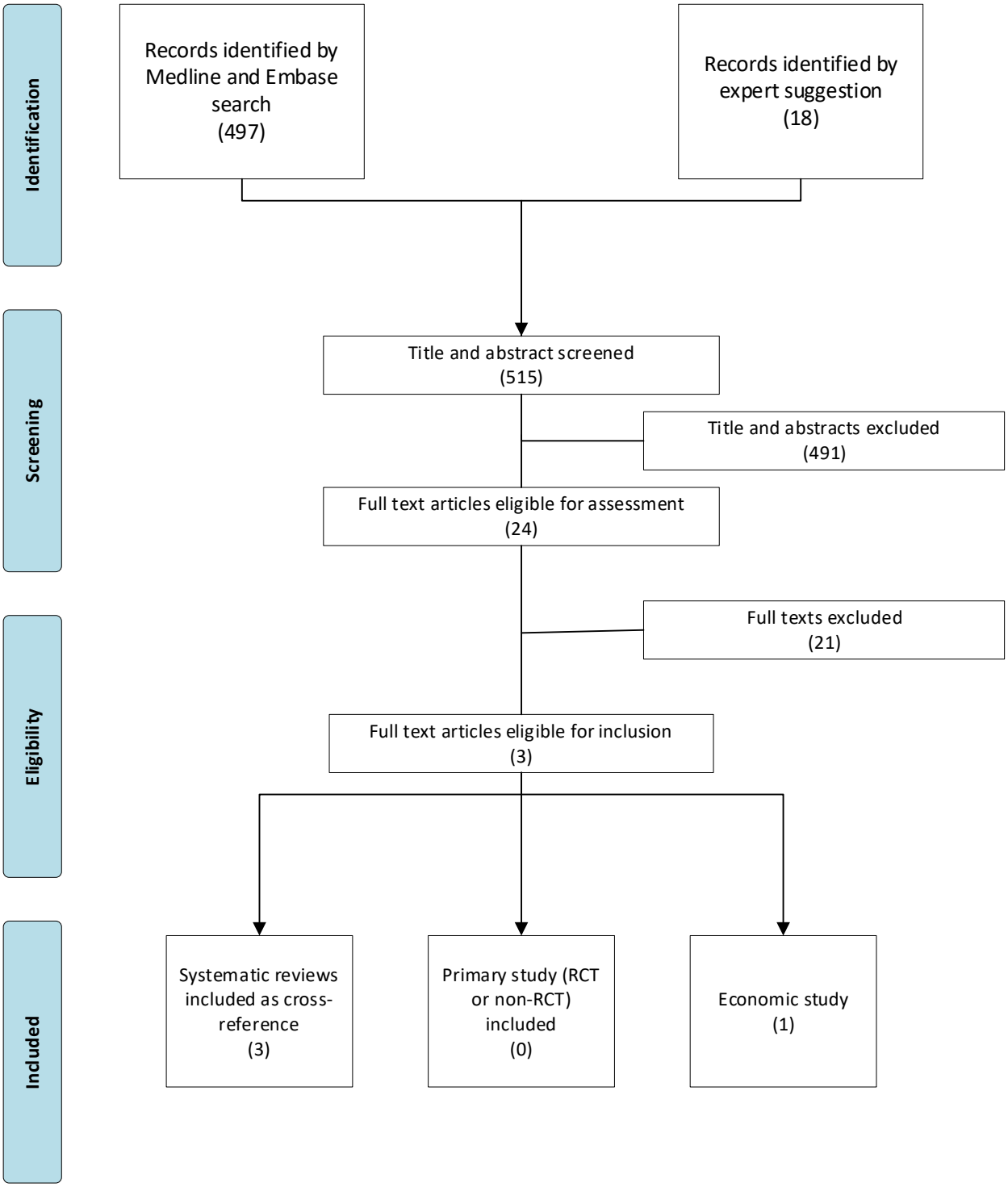
No subgroup analysis was performed.

5.3 Search results

A total of 317 abstracts were screened for clinical review, of which 32 records were retrieved for full text review. No RCT or non-RCT directly comparing Rezum to TURP was identified. Two NMAs were identified indirectly comparing Rezum with several other surgical interventions including TURP.[31, 32]

A total of 180 economic abstracts were screened (one record was identified from other sources), of which 18 duplicates were identified, and five records were retrieved for full text review. From the full texts identified, one study met the inclusion criteria.

Figure 5.1. PRISMA diagram



5.4 Clinical effectiveness

5.4.1 Discussion

No studies (RCT or non-RCT) comparing Rezum to TURP were identified. There were three network meta-analyses indirectly comparing Rezum to TURP.[31-33] Network meta-analysis is a type of indirect comparison which allows interventions to be compared through common comparators. All NMAs only included RCTs to prevent violation of the transitivity assumption. Both utilized the frequentist approach to estimate the effect size and 95% confidence intervals.

Tanneru 2021 provided time specific estimates from one to 24 months; Franco 2021 provided an overall estimate without specific time. Tanneru 2021 found that TURP provided significant benefit over Rezum in IPSS, quality of life, and Qmax (peak flow rate).[31] Rezum was only comparable to TURP in quality of life measurement at one to three months, then TURP provided better quality of life than Rezum after three months. Franco 2021 found that Rezum was not significantly different than TURP in IPSS, quality of life, risk of major adverse events, risk of minor adverse events. Sanja 2021 found that in relation to TURP in the present analysis, the 3-month comparison did not identify any significant differences in IPSS, Qmax, QoL, and postvoid residual.[33]

NMAs may be influenced by the mix of interventions included in the NMA. The two NMAs found different results regarding Rezum and TURP in both IPSS and quality of life. This difference may be due to the NMAs including different interventions and therefore creating different network dynamics. Overall, neither NMA found Rezum provide any clinical benefit over the current standard of care, TURP.

5.5 Cost-effectiveness

One study met the inclusion criteria and an overview of the characteristics and results of the included study is provided below and summarized in

Table 5.2.[34]

5.5.1 Description of included economic studies

The study by Chughtai 2022 was funded by Boston Scientific, the manufacturer of Rezum.[34] The evaluation was conducted from the US Medicare perspective, assessing the cost-effectiveness of five different treatment options:

- Transurethral resection of the prostate (TURP)
- Photoselective vaporization of the prostate (PVP)
- Prostatic urethral lift (PUL)
- Water vapor thermal therapy (WVTT; i.e, Rezum)
- Combination therapy; Defined as a fixed-dose combination of tamsulosin and dutasteride

In their evaluation, Chughtai 2022 evaluated the cost-effectiveness of TURP, PVP, PUL, and Rezum *relative* to combination therapy.

The target population included men (63 years old) with moderate-to-severe LUTS with an average International Prostate Symptom Score (IPSS) of 22, in line with the baseline characteristics of the population enrolled in the Rezum II trial.[26] The economic evaluation took the form of a cost-utility analysis (i.e. cost per QALYS). Treatment effect was modelled as the change in IPSS values relative to baseline. The adjusted IPSS changes for each treatment considered was obtained from a random-effects network meta-analysis (NMA). The NMA was

informed by 20 studies (16 randomized controlled trails, 4 non-randomized trials) that were identified from a systematic review of the literature conducted by the authors. A list of the publications used to inform the NMA, as reported by the authors are included in Appendix E. However, details regarding the analytic approach used to estimate the treatment effect from the NMA were not provided. Overall, the cost categories considered included the cost of the procedures, adverse events (short-term and long-term) and follow-up cost. All cost inputs were informed from Medicare reimbursement rates. All costs were presented in 2021 USD. Health system costs and upfront capital cost for equipment required for each procedure were not considered in the analysis.

Table 5.2 Overview of study characteristics and analytic approach

	Chughtai et al. (2022)
Funding	Boston Scientific
Type of Economic Evaluation	Cost-utility analysis
Target Population	Men with moderate-to-severe LUTS
Interventions	TURP, Rezum, PUL, PVP
Comparator	combination therapy
Analytic Method	Deterministic (reference case)
Modelling	Markov cohort state transition
Effectiveness	Treatment effect was modelled in terms of the change in IPSS relative to baseline and informed by an NMA.
Country	USA
Perspective	US Medicare
Time Horizon	5 years
Discount Rate (Costs & Outcomes)	3%
Cycle length	3-month cycles applied for the first year; 1-year cycles for years 2-5
Reported Outcomes	QALYs
Resource Use and Costs	Costing informed from Medicare reimbursement rate; costing categories included procedural, adverse event & follow-up costs; costs were reported in 2021 USD
Uncertainty/ Sensitivity analysis	Scenario analyses & one-way sensitivity analyses, probabilistic analysis presented as a sensitivity analysis.

NMA= Network meta-analysis PUL=Prostatic urethral lift; PVP= Photoselective vaporization of the prostate; QALYs=Quality-adjusted life years; TURP=Transurethral resection of the prostate

5.5.2 Result of economic literature review

The results as reported by Chughtai 2022are summarized in Table 5.3.

In the primary economic evaluation conducted by Chughtai 2022 over the 5- year time horizon considered, *relative* to CT, Rezum, PVP and TURP were dominant (i.e. cost less and provide more QALYs). The reference cases analysis found that over the five-year time horizon, TURP had the highest total QALYs, followed by PVP, Rezum, PUL and CT. In terms of total costs, PUL had the highest total costs, followed by CT, TURP, PVP and Rezum. In the comparative analysis of the results, Chughtai 2022only compared the results relative to combination therapy, and did not discuss the cost-effectiveness of Rezum relative to TURP. However, in assessment of the model outputs for Rezum versus TURP, Rezum produced less QALYs (4.189 vs 4.246) and was less costly ($2,655 vs. $6,328). Sensitivity analyses were conducted, where the results were only presented relative to combination therapy; the model results were sensitive to changes in utilities, cost parameters and discount rates.

Table 5.3 Summary of result from the identified economic studies- (per person, 2021 USD)

	Generic CT	PUL	REZUM	PVP	TURP
Total Costs	$8,223	$9,580	$2,655	$6,152	$6,328
Total QALYs	4.118	4.141	4.189	4.229	4.246
Incremental cost	*Reference*	$1,357	-$5,568	-$2,071	-$1,895
Incremental QALYs		0.023	0.071	0.11	0.13
Incremental cost per QALY		**$59,000***	**Dominant**	**Dominant**	**Dominant**

CT=combination therapy; PUL=Prostatic urethral lift; PVP= Photoselective vaporization of the prostate; QALYs=Quality-adjusted life years; TURP=Transurethral resection of the prostate

*Note: In the publication by Chughtai 2022a potential calculation error was noted, where the incremental cost/QALY of PUL versus CT was presented as $57,888, however the incremental cost/incremental QALY ($1357/0.023) is equal to $59,000 and thus has been updated in this table

5.5.3 Discussion of findings in the economic studies

5.5.3.1 What is the cost-effectiveness of the technology in the same clinical populations from the previously published economic analysis? Discuss limitations of findings and other aspects relevant to the BC context (if needed)?

The economic review identified one study that evaluated the cost-effectiveness of Rezum (and 3 other treatment options; PUL, PVP and TURP) relative to combination therapy. In this comparative analysis, Rezum was found to be the dominant option, however, this finding is not relevant to the BC context, as TURP is the main comparator to Rezum. In addition, relative to combination therapy TURP was also dominant, and based on the study's findings, TURP is more effective than the Rezum; where over 5 years TURP produced higher total QALYs than Rezum.

The analysis was funded by the manufacturers of Rezum (Boston Scientific) and conducted from the US Medicare perspective, which provides challenges when extrapolating to the Canadian setting and increases the risk of bias, respectively. Further, in estimation of the costs, the authors only included the cost of Medicare reimbursement, which does not comprehensively capture the overall cost incurred by the health care system, such as any upfront capital investment required for the purchasing of devices, device replacements, hospitalization costs, or downstream healthcare utilization costs. Thus, it is likely the cost estimates presented do not accurately reflect the overall cost and resources associated with each treatment options.

In the absence of direct comparative clinical trials of the intervention considered, the authors conducted an NMA to determine a measure for the treatment effect used in the economic model. As this analysis was not part of a separate publication, and detailed

information regarding this analysis was not provided in the methods, it is difficult to assess the robustness (and the extent of the risk of bias) of this effect measure used in the economic analysis. However, like the NMAs identified in the clinical review (see section 5.4.1), it was found that Rezum does *not* provide any clinical benefit over TURP.

5.6 Overall conclusion

The clinical review did not identify any primary study that compared Rezum directly with TURP. Two indirect comparisons that included Rezum and TURP, did not found Rezum providing additional benefit over TURP.[31, 32] In one indirect comparison, TURP was found to provide significant benefit over Rezum in IPSS, quality of life, and peak flow rate measure in Qmax.[31] Both indirect comparison included only RCTs and both identified one RCT that examined Rezum. The certainty of the evidence was low in both indirect comparison due to small sample size from the single RCT.

The economic review did not identify any studies that directly compared the Rezum to TURP. Further, the development of an economic model for BC is not appropriate at this time, as there is a lack of appropriate clinical studies that can demonstrate the clinical utility of Rezum over TURP.

After discussion with HTAO and HTAC regarding the evidence for Rezum, a cost-effectiveness analysis and budget impact analysis were not carried out for this project.

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Appendix A **Semi-structured interview guide for key stakeholder interviews**

1. Tell me a bit about your background.

2. How frequently do you see BPH (benign prostatic hyperplasia) in your practice?

3. What is the current 'best practice' or standard of treatment for BPH, and what is the 'status quo' in BC with respect to delivering that standard of care?

4. What new or emerging technologies for treating this condition are you aware of?

5. On Rezum particularly…

-do you use or have you used this technology? If yes, what have you observed for patient outcomes and satisfaction?

-who are you aware, in BC or elsewhere, who uses this technology?

-for what populations would it best be used?

-is there likely to be increased use of the technology in BC in the near- to medium-term? What factors would drive this usage, or lack of uptake?

Appendix B **Search Strategies**

B.1 Clinical

Ovid Multifile

Database: EBM Reviews - Database of Abstracts of Reviews of Effects <1st Quarter 2016>, EBM Reviews - Health Technology Assessment <4th Quarter 2016>, Embase <1974 to 2022 February 16>, EBM Reviews - Cochrane Central Register of Controlled Trials <January 2022>, EBM Reviews - Cochrane Database of Systematic Reviews <2005 to February 16, 2022>, Ovid MEDLINE(R) ALL <1946 to February 16, 2022>
Search Strategy:
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1 Rezum$2.tw,kw,kf. [REZUM] (432)
2 Prostatic Hyperplasia/ (46294)
3 Prostatism/ (1552)
4 Lower Urinary Tract Symptoms/ (12879)
5 prostatism*.tw,kw,kf. (1388)
6 (prostat* adj3 (enlarg* or large or larger or hyperplasia* or hyper-plasia* or hypertroph* or hyper-troph* or obstruct*)).tw,kw,kf. (65231)
7 ((BPE or BPO or BPH) and prostat*).tw,kw,kf. (32237)
8 (lower urinary tract adj3 (disease* or disorder* or dysfunction* or symptom*)).tw,kw,kf. (33810)
9 ((LUDS or LUTS or MLUDS or MLUTS) and (lower or urinary or urine or urination)).tw,kw,kf. (15433)
10 or/2-9 [BPH, LUTS] (106979)
11 Steam/ (15737)
12 (vapo?r* thermal adj3 (ablat* or energy or therap* or treat*)).tw,kw,kf. (224)
13 (water vapo?r* adj3 (ablat* or energy or therap* or treat*)).tw,kw,kf. (595)
14 (steam* adj3 (ablat* or energy or therap* or treat*)).tw,kw,kf. (1807)
15 (vapo?r* ablat* adj3 prostat*).tw,kw,kf. (9)
16 (water ablat* adj3 prostat*).tw,kw,kf. (1)
17 or/11-16 [WATER VAPOUR/STEAM THERAPY] (17135)
18 10 and 17 [BPH, LUTS - WATER VAPOUR/STEAM] (368)
19 1 or 18 [REZUM, BPH, LUTS - WATER VAPOUR/STEAM THERAPY] (523)
20 exp Animals/ not Humans/ (17067027)
21 19 not 20 [ANIMAL-ONLY REMOVED] (446)
22 21 use medall [MEDLINE RECORDS] (158)
23 Rezum$2.dv,tw,kw,kf. [REZUM] (439)
24 prostate hypertrophy/ (38980)
25 prostatism/ (1552)
26 lower urinary tract symptom/ (21210)
27 prostatism*.tw,kw,kf. (1388)
28 (prostat* adj3 (enlarg* or large or larger or hyperplasia* or hyper-plasia* or hypertroph* or hyper-troph* or obstruct*)).tw,kw,kf. (65231)
29 ((BPE or BPO or BPH) and prostat*).tw,kw,kf. (32237)
30 (lower urinary tract adj3 (disease* or disorder* or dysfunction* or symptom*)).tw,kw,kf. (33810)
31 ((LUDS or LUTS or MLUDS or MLUTS) and (lower or urinary or urine or urination)).tw,kw,kf. (15433)
32 or/24-31 [BPH, LUTS] (106120)
33 water vapor/ (15737)
34 (vapo?r* thermal adj3 (ablat* or energy or therap* or treat*)).tw,kw,kf. (224)
35 (water vapo?r* adj3 (ablat* or energy or therap* or treat*)).tw,kw,kf. (595)
36 (steam* adj3 (ablat* or energy or therap* or treat*)).tw,kw,kf. (1807)
37 (vapo?r* ablat* adj3 prostat*).tw,kw,kf. (9)
38 (water ablat* adj3 prostat*).tw,kw,kf. (1)

39 or/33-38 [WATER VAPOUR/STEAM THERAPY] (17135)
40 32 and 39 [BPH, LUTS - WATER VAPOUR/STEAM] (372)
41 23 or 40 [REZUM, BPH, LUTS - WATER VAPOUR/STEAM THERAPY] (531)
42 exp animal/ or exp animal experimentation/ or exp animal model/ or exp animal experiment/ or nonhuman/ or exp vertebrate/ (55912390)
43 exp human/ or exp human experimentation/ or exp human experiment/ (44098640)
44 42 not 43 (11815525)
45 41 not 44 [ANIMAL-ONLY REMOVED] (529)
46 45 use oemezd [EMBASE RECORDS] (300)
47 Rezum$2.mp. [REZUM] (444)
48 Prostatic Hyperplasia/ (46294)
49 Prostatism/ (1552)
50 Lower Urinary Tract Symptoms/ (12879)
51 prostatism*.ti,ab,kw. (1379)
52 (prostat* adj3 (enlarg* or large or larger or hyperplasia* or hyper-plasia* or hypertroph* or hyper-troph* or obstruct*)).ti,ab,kw. (63149)
53 ((BPE or BPO or BPH) and prostat*).ti,ab,kw. (31978)
54 (lower urinary tract adj3 (disease* or disorder* or dysfunction* or symptom*)).ti,ab,kw. (32386)
55 ((LUDS or LUTS or MLUDS or MLUTS) and (lower or urinary or urine or urination)).ti,ab,kw. (15171)
56 or/48-55 [BPH, LUTS] (105510)
57 Steam/ (15737)
58 (vapo?r* thermal adj3 (ablat* or energy or therap* or treat*)).ti,ab,kw. (216)
59 (water vapo?r* adj3 (ablat* or energy or therap* or treat*)).ti,ab,kw. (582)
60 (steam* adj3 (ablat* or energy or therap* or treat*)).ti,ab,kw. (1773)
61 (vapo?r* ablat* adj3 prostat*).ti,ab,kw. (9)
62 (water ablat* adj3 prostat*).ti,ab,kw. (1)
63 or/57-62 [WATER VAPOUR/STEAM THERAPY] (17101)
64 56 and 63 [BPH, LUTS - WATER VAPOUR/STEAM] (354)
65 47 or 64 [REZUM, BPH, LUTS - WATER VAPOUR/STEAM THERAPY] (523)
66 65 use cctr [CENTRAL RECORDS] (64)
67 Rezum$2.mp. [REZUM] (444)
68 prostatism*.ti,ab,kw. (1379)
69 (prostat* adj3 (enlarg* or large or larger or hyperplasia* or hyper-plasia* or hypertroph* or hyper-troph* or obstruct*)).ti,ab,kw. (63149)
70 ((BPE or BPO or BPH) and prostat*).ti,ab,kw. (31978)
71 (lower urinary tract adj3 (disease* or disorder* or dysfunction* or symptom*)).ti,ab,kw. (32386)
72 ((LUDS or LUTS or MLUDS or MLUTS) and (lower or urinary or urine or urination)).ti,ab,kw. (15171)
73 or/68-72 [BPH, LUTS] (89037)
74 (vapo?r* thermal adj3 (ablat* or energy or therap* or treat*)).ti,ab,kw. (216)
75 (water vapo?r* adj3 (ablat* or energy or therap* or treat*)).ti,ab,kw. (582)
76 (steam* adj3 (ablat* or energy or therap* or treat*)).ti,ab,kw. (1773)
77 (vapo?r* ablat* adj3 prostat*).ti,ab,kw. (9)
78 (water ablat* adj3 prostat*).ti,ab,kw. (1)
79 or/74-78 [WATER VAPOUR/STEAM THERAPY] (2355)
80 73 and 79 [BPH, LUTS - WATER VAPOUR/STEAM] (326)
81 67 or 80 [REZUM, BPH, LUTS - WATER VAPOUR/STEAM THERAPY] (509)
82 81 use coch [CDSR RECORDS] (5)
83 Rezum$2.mp. [REZUM] (444)
84 Prostatic Hyperplasia/ (46294)
85 Prostatism/ (1552)
86 Lower Urinary Tract Symptoms/ (12879)
87 prostatism*.tw. (1277)
88 (prostat* adj3 (enlarg* or large or larger or hyperplasia* or hyper-plasia* or hypertroph* or hyper-troph* or

obstruct*)).tw. (62909)
89 ((BPE or BPO or BPH) and prostat*).tw. (31534)
90 (lower urinary tract adj3 (disease* or disorder* or dysfunction* or symptom*)).tw. (32252)
91 ((LUDS or LUTS or MLUDS or MLUTS) and (lower or urinary or urine or urination)).tw. (14830)
92 or/84-91 [BPH, LUTS] (105134)
93 Steam/ (15737)
94 (vapo?r* thermal adj3 (ablat* or energy or therap* or treat*)).tw. (221)
95 (water vapo?r* adj3 (ablat* or energy or therap* or treat*)).tw. (569)
96 (steam* adj3 (ablat* or energy or therap* or treat*)).tw. (1757)
97 (vapo?r* ablat* adj3 prostat*).tw. (7)
98 (water ablat* adj3 prostat*).tw. (1)
99 or/93-98 [WATER VAPOUR/STEAM THERAPY] (17088)
100 92 and 99 [BPH, LUTS - WATER VAPOUR/STEAM] (355)
101 83 or 100 [REZUM, BPH, LUTS - WATER VAPOUR/STEAM THERAPY] (523)
102 101 use clhta,dare [HTA, DARE RECORDS] (0)
103 22 or 46 or 66 or 82 or 102 [ALL DATABASES] (527)
104 remove duplicates from 103 (331) [TOTAL UNIQUE RECORDS]
105 104 use medall [MEDLINE UNIQUE RECORDS] (156)
106 104 use oemezd [EMBASE UNIQUE RECORDS] (153)
107 104 use cctr [CENTRAL UNIQUE RECORDS] (17)
108 104 use coch [CDSR UNIQUE RECORDS] (5)
109 104 use clhta [HTA UNIQUE RECORDS] (0)
110 104 use dare [DARE UNIQUE RECORDS] (0)

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B.2 Economics

Ovid Multifile

Database: EBM Reviews - Health Technology Assessment <4th Quarter 2016>, EBM Reviews - NHS Economic Evaluation Database <1st Quarter 2016>, Embase <1974 to 2022 February 16>, Ovid MEDLINE(R) ALL <1946 to February 16, 2022>
Search Strategy:
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1 Rezum$2.tw,kw,kf. [REZUM] (369)
2 Prostatic Hyperplasia/ (44506)
3 Prostatism/ (1491)
4 Lower Urinary Tract Symptoms/ (12474)
5 prostatism*.tw,kw,kf. (1254)
6 (prostat* adj3 (enlarg* or large or larger or hyperplasia* or hyper-plasia* or hypertroph* or hyper-troph* or obstruct*)).tw,kw,kf. (61062)
7 ((BPE or BPO or BPH) and prostat*).tw,kw,kf. (29913)
8 (lower urinary tract adj3 (disease* or disorder* or dysfunction* or symptom*)).tw,kw,kf. (31109)
9 ((LUDS or LUTS or MLUDS or MLUTS) and (lower or urinary or urine or urination)).tw,kw,kf. (14054)
10 or/2-9 [BPH, LUTS] (100920)
11 Steam/ (15699)
12 (vapo?r* thermal adj3 (ablat* or energy or therap* or treat*)).tw,kw,kf. (183)
13 (water vapo?r* adj3 (ablat* or energy or therap* or treat*)).tw,kw,kf. (523)
14 (steam* adj3 (ablat* or energy or therap* or treat*)).tw,kw,kf. (1734)
15 (vapo?r* ablat* adj3 prostat*).tw,kw,kf. (8)
16 (water ablat* adj3 prostat*).tw,kw,kf. (1)
17 or/11-16 [WATER VAPOUR/STEAM THERAPY] (16972)

18 10 and 17 [BPH, LUTS - WATER VAPOUR/STEAM] (312)
19 1 or 18 [REZUM, BPH, LUTS - WATER VAPOUR/STEAM THERAPY] (452)
20 exp Animals/ not Humans/ (17067021)
21 19 not 20 [ANIMAL-ONLY REMOVED] (375)
22 Economics/ or exp "Costs and Cost Analysis"/ or Economics, Nursing/ or Economics, Medical/ or Economics, Pharmaceutical/ or exp Economics, Hospital/ or Economics, Dental/ or exp "Fees and Charges"/ or exp Budgets/ or exp models, economic/ or markov chains/ or monte carlo method/ or exp Decision Theory/ or (economic$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$ or pharmaco-economic$ or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ti,kf. or ((cost$ adj2 (effective$ or utilit$ or benefit$ or minimi$ or analy$ or outcome or outcomes)) or economic model$).ab,kf. or ((value adj2 (money or monetary)) or markov or monte carlo or budget$ or (decision$ adj2 (tree$ or analy$ or model$))).ti,ab,kf. (2153844)
23 (economic$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$ or pharmaco-economic$ or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ab. /freq=2 (807023)
24 22 or 23 [CADTH ECON FILTER] (2419179)
25 Prostatic Hyperplasia/ec [economics] (194)
26 Prostatism/ec [economics] (3)
27 Lower Urinary Tract Symptoms/ec [economics] (16)
28 or/25-27 [ADDITIONAL ECONOMICS] (204)
29 24 or 28 [ECONOMIC FILTERS] (2419195)
30 21 and 29 [REZUM, BPH, LUTS - WATER VAPOUR/STEAM THERAPY - ECONOMICS] (53)
31 "Value of Life"/ or Quality of Life/ or Quality-Adjusted Life Years/ or exp Health Status/ or exp Health Status Indicators/ or Health Surveys/ (1870587)
32 quality of life.ti,kf. (261768)
33 ((instrument or instruments) adj3 quality of life).ab. (8746)
34 (quality adjusted life or qaly* or qald* or qale* or qtime* or life year or life years or disability adjusted life or daly*).ti,ab,kf. (66101)
35 (sf36 or sf 36 or short form 36 or shortform 36 or short form36 or shortform36 or sf thirtysix or sfthirtysix or sfthirty six or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).ti,ab,kf. (74579)
36 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six or shortform6 or short form6).ti,ab,kf. (5080)
37 (sf8 or sf 8 or sf eight or sfeight or shortform 8 or shortform 8 or shortform8 or short form8 or shortform eight or short form eight).ti,ab,kf. (1519)
38 (sf12 or sf 12 or short form 12 or shortform 12 or short form12 or shortform12 or sf twelve or sftwelve or shortform twelve or short form twelve).ti,ab,kf. (17760)
39 (sf16 or sf 16 or short form 16 or shortform 16 or short form16 or shortform16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).ti,ab,kf. (99)
40 (sf20 or sf 20 or short form 20 or shortform 20 or short form20 or shortform20 or sf twenty or sftwenty or shortform twenty or short form twenty).ti,ab,kf. (919)
41 (hql or hqol or h qol or hrqol or hr qol or hye or hyes).ti,ab,kf. (55196)
42 (health* adj2 year* adj2 equivalent*).ti,ab,kf. (103)
43 (pqol or qls).ti,ab,kf. (1117)
44 (quality of wellbeing or quality of well being or index of wellbeing or index of well being or qwb).ti,ab,kf. (1467)
45 nottingham health profile*.ti,ab,kf. (2814)
46 sickness impact profile.ti,ab,kf. (2351)
47 (health adj3 (utilit* or status)).ti,ab,kf. (190848)
48 (utilit* adj3 (valu* or measur* or health or life or estimat* or elicit* or disease or score* or weight)).ti,ab,kf. (36892)
49 (preference* adj3 (valu* or measur* or health or life or estimat* or elicit* or disease or score* or instrument or instruments)).ti,ab,kf. (29443)

50 (disutilit* or rosser or willingness to pay or standard gamble* or time trade off or time tradeoff or tto or hui or hui1 or hui2 or hui3 or eq or euroqol or euro qol or eq5d or eq 5d or euroqual or euro qual or duke health profile or functional status questionnaire or dartmouth coop functional health assessment* or WHOQOL or WHOQOL-BREF or Functional Assessment of Chronic Illness Therapy or discrete choice experiment?).tw,kf. (96264)
51 (International Prostatic Symptom Score or IPSS).ti,ab,kf. (19732)
52 (BPH-QOL9 or BPH-QOL-9 or BPH-QOL20 or BPH-QOL-20).ti,ab,kf. (7)
53 or/31-52 [HEALTH UTILITIES/QOL FILTER] (2122343)
54 21 and 53 [REZUM, BPH, LUTS - WATER VAPOUR/STEAM THERAPY - QOL] (151)
55 30 or 54 [REZUM - ECON, QOL] (179)
56 55 use medall [MEDLINE RECORDS] (58)
57 Rezum$2.dv,tw,kw,kf. [REZUM] (376)
58 prostate hypertrophy/ (38980)
59 prostatism/ (1491)
60 lower urinary tract symptom/ (20803)
61 prostatism*.tw,kw,kf. (1254)
62 (prostat* adj3 (enlarg* or large or larger or hyperplasia* or hyper-plasia* or hypertroph* or hyper-troph* or obstruct*)).tw,kw,kf. (61062)
63 ((BPE or BPO or BPH) and prostat*).tw,kw,kf. (29913)
64 (lower urinary tract adj3 (disease* or disorder* or dysfunction* or symptom*)).tw,kw,kf. (31109)
65 ((LUDS or LUTS or MLUDS or MLUTS) and (lower or urinary or urine or urination)).tw,kw,kf. (14054)
66 or/58-65 [BPH, LUTS] (100292)
67 water vapor/ (15699)
68 (vapo?r* thermal adj3 (ablat* or energy or therap* or treat*)).tw,kw,kf. (183)
69 (water vapo?r* adj3 (ablat* or energy or therap* or treat*)).tw,kw,kf. (523)
70 (steam* adj3 (ablat* or energy or therap* or treat*)).tw,kw,kf. (1734)
71 (vapo?r* ablat* adj3 prostat*).tw,kw,kf. (8)
72 (water ablat* adj3 prostat*).tw,kw,kf. (1)
73 or/67-72 [WATER VAPOUR/STEAM THERAPY] (16972)
74 66 and 73 [BPH, LUTS - WATER VAPOUR/STEAM] (316)
75 57 or 74 [REZUM, BPH, LUTS - WATER VAPOUR/STEAM THERAPY] (460)
76 exp animal/ or exp animal experimentation/ or exp animal model/ or exp animal experiment/ or nonhuman/ or exp vertebrate/ (55293905)
77 exp human/ or exp human experimentation/ or exp human experiment/ (43480172)
78 76 not 77 (11815508)
79 75 not 78 [ANIMAL-ONLY REMOVED] (458)
80 economics/ or cost/ or exp health economics/ or exp budget/ or statistical model/ or probability/ or monte carlo method/ or decision theory/ or decision tree/ or (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ti,kw. or ((cost$ adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)) or economic model*).ab,kw. or ((value adj2 (money or monetary)) or markov or monte carlo or budget* or (decision* adj2 (tree* or analy* or model*))).ti,ab,kw. (3742600)
81 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ab. /freq=2 (807023)
82 80 or 81 [CADTH ECON FILTER] (3994624)
83 79 and 82 [REZUM, BPH, LUTS - WATER VAPOUR/STEAM THERAPY - ECON] (64)
84 socioeconomics/ or exp quality of life/ or quality-adjusted life year/ or nottingham health profile/ or sickness impact profile/ or health status indicator/ or health status/ or functional status/ or health survey/ (1430913)
85 quality of life.ti,kw. (251827)
86 ((instrument or instruments) adj3 quality of life).ab. (8746)
87 (quality adjusted life or qaly* or qald* or qale* or qtime* or life year or life years or disability adjusted life or daly*).ti,ab,kw. (65625)
88 (sf36 or sf 36 or short form 36 or shortform 36 or short form36 or shortform36 or sf thirtysix or sfthirtysix or

sfthirty six or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).ti,ab,kw. (74401)
89 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six or shortform6 or short form6).ti,ab,kw. (5064)
90 (sf8 or sf 8 or sf eight or sfeight or shortform 8 or shortform 8 or shortform8 or short form8 or shortform eight or short form eight).ti,ab,kw. (1511)
91 (sf12 or sf 12 or short form 12 or shortform 12 or short form12 or shortform12 or sf twelve or sftwelve or shortform twelve or short form twelve).ti,ab,kw. (17713)
92 (sf16 or sf 16 or short form 16 or shortform 16 or short form16 or shortform16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).ti,ab,kw. (99)
93 (sf20 or sf 20 or short form 20 or shortform 20 or short form20 or shortform20 or sf twenty or sftwenty or shortform twenty or short form twenty).ti,ab,kw. (917)
94 (hql or hqol or h qol or hrqol or hr qol or hye or hyes).ti,ab,kw. (54870)
95 (health* adj2 year* adj2 equivalent*).ti,ab,kw. (100)
96 (pqol or qls).ti,ab,kw. (1113)
97 (quality of wellbeing or quality of well being or index of wellbeing or index of well being or qwb).ti,ab,kw. (1458)
98 nottingham health profile*.ti,ab,kw. (2812)
99 sickness impact profile.ti,ab,kw. (2346)
100 (health adj3 (utilit* or status)).ti,ab,kw. (186619)
101 (utilit* adj3 (valu* or measur* or health or life or estimat* or elicit* or disease or score* or weight)).ti,ab,kw. (36745)
102 (preference* adj3 (valu* or measur* or health or life or estimat* or elicit* or disease or score* or instrument or instruments)).ti,ab,kw. (29312)
103 (disutilit* or rosser or willingness to pay or standard gamble* or time trade off or time tradeoff or tto or hui or hui1 or hui2 or hui3 or eq or euroqol or euro qol or eq5d or eq 5d or euroqual or euro qual or duke health profile or functional status questionnaire or dartmouth coop functional health assessment* or WHOQOL or WHOQOL-BREF or Functional Assessment of Chronic Illness Therapy or discrete choice experiment?).ti,ab,kw. (94086)
104 (International Prostatic Symptom Score or IPSS).ti,ab,kw. (19676)
105 (BPH-QOL9 or BPH-QOL-9 or BPH-QOL20 or BPH-QOL-20).ti,ab,kw. (7)
106 or/84-105 [HEALTH UTILITIES/QOL FILTER] (1687085)
107 79 and 106 [REZUM, BPH, LUTS - WATER VAPOUR/STEAM THERAPY - QOL] (187)
108 83 or 107 [REZUM - ECON, QOL] (221)
109 108 use oemezd [EMBASE SEARCH] (162)
110 Rezum$2.mp. [REZUM] (381)
111 Prostatic Hyperplasia/ (44506)
112 Prostatism/ (1491)
113 Lower Urinary Tract Symptoms/ (12474)
114 prostatism*.tw. (1215)
115 (prostat* adj3 (enlarg* or large or larger or hyperplasia* or hyper-plasia* or hypertroph* or hyper-troph* or obstruct*)).tw. (58956)
116 ((BPE or BPO or BPH) and prostat*).tw. (29238)
117 (lower urinary tract adj3 (disease* or disorder* or dysfunction* or symptom*)).tw. (29776)
118 ((LUDS or LUTS or MLUDS or MLUTS) and (lower or urinary or urine or urination)).tw. (13500)
119 or/111-118 [BPH, LUTS] (99338)
120 Steam/ (15699)
121 (vapo?r* thermal adj3 (ablat* or energy or therap* or treat*)).tw. (180)
122 (water vapo?r* adj3 (ablat* or energy or therap* or treat*)).tw. (505)
123 (steam* adj3 (ablat* or energy or therap* or treat*)).tw. (1684)
124 (vapo?r* ablat* adj3 prostat*).tw. (6)
125 (water ablat* adj3 prostat*).tw. (1)
126 or/120-125 [WATER VAPOUR/STEAM THERAPY] (16931)

127 119 and 126 [BPH, LUTS - WATER VAPOUR/STEAM] (299)
128 110 or 127 [REZUM, BPH, LUTS - WATER VAPOUR/STEAM THERAPY] (452)
129 128 use clhta,cleed [HTA, NHS EED RECORDS] (0)
130 56 or 109 or 129 [ALL DATABASES] (220)
131 remove duplicates from 130 [TOTAL UNIQUE RECORDS] (165)
132 131 use medall [MEDLINE UNIQUE RECORDS] (57)
133 131 use oemezd [EMBASE UNIQUE RECORDS] (108)
134 131 use cleed,clhta [HTA, NHS EED UNIQUE RECORDS] (0)

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Appendix C **List of excluded studies**

C.1 Clinical reviews

AUTHOR	YEAR	TITLE	JOURNAL	VOLUME	ISSUE	PAGE	REASON FOR EXCLUSION
Checcucci, E.	2021	New Ultra-minimally Invasive Surgical Treatment for Benign Prostatic Hyperplasia: A Systematic Review and Analysis of Comparative Outcomes	European Urology Open Science	33		28-41	Did not compare Rezum to TURP
Dahm, P.	2021	Newer Minimally Invasive Treatment Modalities to Treat Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia	European Urology Open Science	26		72-82	Did not compare Rezum to TURP
Hamed, L.	2021	Minimally invasive and endoscopic therapies of benign prostatic hyperplasia (BPH): Head-to-head comparison of short-term outcomes by multiple treatments (Network) meta-analysis	Journal of Endourology	35(SUPPL 1)		A28-A29	Conference abstract
Manfredi, C.	2021	Emerging minimally invasive transurethral treatments for benign prostatic hyperplasia: a systematic review with meta-analysis of functional outcomes and description of complications	Minerva Urology and Nephrology	26		26	Did not compare Rezum to TURP
McVary, K.T.	2021	Preservation of Sexual Function 5 Years After Water Vapor Thermal Therapy for Benign Prostatic Hyperplasia	Sexual Medicine	9	6	100454	RCT with sham control
McVary, K.T.	2021	Final 5-Year Outcomes of the	Journal of Urology	206	3	715-724	RCT with sham control

		Multicenter Randomized Sham-Controlled Trial of a Water Vapor Thermal Therapy for Treatment of Moderate to Severe Lower Urinary Tract Symptoms Secondary to Benign Prostatic Hyperplasia					
Sajan, A.	2021	Minimally Invasive Treatments for Benign Prostatic Hyperplasia: Systematic Review and Network Meta-Analysis	Journal of Vascular & Interventional Radiology	27		27	SR for cross reference
Ting, A.	2021	Minimally invasive surgical treatment of benign prostatic hyperplasia: A systematic review	British Journal of Surgery	108(SUPPL 6)		vi281	Conference abstract
Ting, A.	2021	Minimally invasive surgical treatment of benign prostatic hyperplasia: A systematic review	Journal of Endourology	35(SUPPL 1)		A28	Conference abstract
Johnston, M.J.	2020	Rezum water vapour therapy: promising early outcomes from the first UK series	BJU International	126	5	557-558	Not research article
Kang, T.W.	2020	Convective radiofrequency water vapour thermal therapy for lower urinary tract symptoms in men with benign prostatic hyperplasia	Cochrane Database of Systematic Reviews	3		CD013251	SR with sham control
Tanneru, K.	2020	An indirect comparison of newer minimally invasive treatments for benign prostatic hyperplasia: A network meta-analysis model	International Journal of Urology	27(SUPPL 1)		132	Conference abstract
Martinelli, E.	2018	[The Rezum system in the treatment of male lower urinary tract symptoms	Aktuelle Urologie	49	6	e94	Not English

		(LUTSs) due to benign prostatic obstruction (BPO)]					
McVary, K.T.	2018	Comparison of convective radiofrequency thermal therapy of prostate (REZ}UMC) to MTOPS study cohort sexual function response at 3 years	Journal of Endourology	32(Supplement 2)		A392-A393	Conference abstract
Roehrborn, C.G.	2017	Convective Thermal Therapy: Durable 2-Year Results of Randomized Controlled and Prospective Crossover Studies for Treatment of Lower Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia	Journal of Urology	197	6	1507-1516	RCT with sham control
McVary, K.T.	2016	Erectile and Ejaculatory Function Preserved With Convective Water Vapor Energy Treatment of Lower Urinary Tract Symptoms Secondary to Benign Prostatic Hyperplasia: Randomized Controlled Study	Journal of Sexual Medicine	13	6	924-33	RCT with sham control

McVary, K.T.	2016	Minimally Invasive Prostate Convective Water Vapor Energy Ablation: A Multicenter, Randomized, Controlled Study for the Treatment of Lower Urinary Tract Symptoms Secondary to Benign Prostatic Hyperplasia	Journal of Urology	195	5	1529-1538	RCT with sham control	

C.2 Economic review

AUTHOR	YEAR	TITLE	JOURNAL	VOLUME	ISSUE	PAGE	REASON FOR EXCLUSION
Haroon, U.M., Khan, J.S., McNicholas, D., Forde, J.C., Davis, N.F. and Power, R.E.	2022	Introduction of Rezum system technology to Ireland for treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia: a pilot study on early outcomes and procedure cost analysis	Irish Journal of Medical Science	191	1	421-426	study design
Chughtai, B., Rojanasarot, S., Neeser, K., Gultyaev, D., Amorosi, S.L. and Shore, N.D.	2021	Cost-Effectiveness and Budget Impact of Emerging Minimally Invasive Surgical Treatments for Benign Prostatic Hyperplasia	Journal of Health Economics &	8	1	42-50	study design

			Outcomes Research			
Shabataev, V., Allahwala, A. and Elterman, D.S.	2019	Cost-effectiveness of Medical Versus Surgical Therapy for BPH	Current Bladder Dysfunction Reports	14(1)	13-17	Intervention
Aladesuru, O., Punyala, A., Stoddard, M., Bhojani, N., Zorn, K., Elterman, D. and Chughtai, B.	2022	Review of the Economics of Surgical Treatment Options for Benign Prostatic Hyperplasia	Current Urology Reports	14	14	Intervention

Appendix D **Description of the included studies**

Study	Descriptions
Tannaru 2021[31]	This study was designed to provide an indirect comparison of the urinary and sexual domain outcomes and complications after newer minimally invasive surgical therapy (MIST) of Aquablation, Rezum, and UroLift for benign prostatic hyperplasia (BPH) for transurethral resection of prostate (TURP). A total of four RCTs reporting the outcomes after treatment with newer MIST for BPH were identified. Aquablation and TURP necessitate general or regional anesthesia and both produced significantly better urinary domain scores compared to Rezum and UroLift. On the other hand, UroLift demonstrated better sexual function domain scores compared to TURP, but not Aquablation. There was no significant difference in urinary domain scores between UroLift and Rezum at 24 months of follow-up.
Franco 2021[32]	The primary objective was to assess the comparative effectiveness of minimally invasive treatments for lower urinary tract symptoms in men with BPH through a network meta-analysis. Our secondary objective was to obtain an estimate of relative ranking of these minimally invasive treatments, according to their effects. Interventions included convective radiofrequency water vapor therapy (CRFWVT); prostatic arterial embolization (PAE); prostatic urethral lift (PUL); temporary implantable nitinol device (TIND); and transurethral microwave thermotherapy (TUMT). The report included 27 trials involving 3017 men, mostly over age 50, with severe LUTS due to BPH. The overall certainty of evidence was low to very low due to concerns regarding bias, imprecision, inconsistency (heterogeneity), and incoherence. Minimally invasive treatments may result in similar or worse effects concerning urinary symptoms and QoL compared to TURP at short-term follow-up. They may also result in fewer major adverse events.
Sanja 2021[33]	The objective of this report was to review and to compare indirectly the outcomes of minimally invasive therapies for the treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia. Interventions included were Rezum, Urolift, Aquablation, and prostatic artery embolization (PAE). Data on the following variables were included: International prostate symptom score (IPSS), maximum urinary flow rate, quality of life, and postvoid residual (PVR). There was no significant difference in outcomes between therapies for IPSS at the 3, 6, and 12-month follow ups. Although outcomes for Rezum were only available out to 3 months, there were no consistently significant differences in outcomes when comparing Aquablation versus PAE versus Rezum. TURP PVR was significantly better than Urolift at 3, 6, and 12 months. No significant differences in minor or major adverse events were noted. Although significant differences in outcomes were limited, Aquablation and PAE were the most durable at 12 months. PAE has been well studied on multiple randomized control trials with minimal adverse events while Aquablation has limited high quality data and has been associated with bleeding-related complications.

Appendix E **List of studies included in the NMA presented in Chughtai 2021** [35]

Full-Text Citations	
1	Yoon C.J., Kim J.Y., Moon K.H., et al. Transurethral resection of the prostate with a bipolar tissue management system compared to conventional monopolar resectoscope: One-year outcome. Yonsei Med J. 2006;47(5):715-20.
2	Tugcu V., Tasci A.I., Sahin S., et al. Comparison of photoselective vaporization of the prostate and transurethral resection of the prostate: A prospective nonrandomized bicenter trial with 2-year follow-up. J Endourol. 2008;22(7):1519-25.
3	Autorino R., Damiano R., Di Lorenzo G., et al. Four-year outcome of a prospective randomised trial comparing bipolar plasmakinetic and monopolar transurethral resection of the prostate. Eur Urol. 2009;55(4):922-9.
4	Bouchier-Hayes D.M., Van Appledorn S., Bugeja P., et al. A randomized trial of photoselective vaporization of the prostate using the 80-W potassium-titanyl-phosphate laser vs transurethral prostatectomy, with a 1-year follow-up. BJU Int. 2010;105(7):964-9.
5	Elmansy H.M., Elzayat E., Elhilali M.M. Holmium laser ablation versus photoselective vaporization of prostate less than 60 cc: Long-term results of a randomized trial. J Urol. 2010;184(5):2023-8.
6	Singhania P., Nandini D., Sarita F., et al. Transurethral resection of prostate: A comparison of standard monopolar versus bipolar saline resection. Int Braz J Urol. 2010;36(2):183-9.
7	Akman T., Binbay M., Tekinarslan E., et al. Effects of bipolar and monopolar transurethral resection of the prostate on urinary and erectile function: A prospective randomized comparative study. BJU Int. 2013;111(1):129-36.
8	Hamouda A.G.M., Morsi G., Habib E., et al. A comparative study between holmium laser enucleation of the prostate and transurethral resection of the prostate: 12-month follow-up. J Clin Urol. 2014;7(2):99-104.
9	Bachmann A., Tubaro A., Barber N., et al. A European multicenter randomized noninferiority trial comparing GreenLight XPS laser vaporization and transurethral resection of the prostate for the treatment of benign prostatic obstruction: 12-month results of the GOLIATH study. J Urol. 2015;193(2):570-8
10	Sonksen J., Barber N.J., Speakman M.J., et al. Prospective, randomized, multinational study of prostatic urethral lift versus transurethral resection of the prostate: 12-month results from the BPH6 study. Eur Urol. 2015;68(4):643-52.
11	Guo S., Muller G., Lehmann K., et al. The 80-W KTP GreenLight laser vaporization of the prostate versus transurethral resection of the prostate (TURP): Adjusted analysis of 5-year results of a prospective non-randomized bi-center study. Lasers Med Sci. 2015;30(3):1147-51.
12	Thomas J.A., Tubaro A., Barber N., et al. A multicenter randomized noninferiority trial comparing GreenLight-XPS Laser vaporization of the prostate and transurethral resection of the prostate for the treatment of benign prostatic obstruction: Two-yr outcomes of the GOLIATH study. Eur Urol. 2016;69(1):94-102.
13	Al-Rawashdah S.F., Pastore A.L., Salhi Y.A., et al. Prospective randomized study comparing monopolar with bipolar transurethral resection of prostate in benign prostatic obstruction: 36-month outcomes. J Urol. 2017;35(10):1595-601.
14	Purkait B., Sinha R.J., Srinivas K.S.A., et al. Outcome analysis of transurethral resection versus potassium titanyl phosphate-photo selective vaporization of the prostate for the treatment of benign prostatic hyperplasia; A randomized controlled trial with 4 years follow up. Turk J Urol. 2017;43(2):176-82.
15	Roehrborn C.G., Barkin J., Gange S.N., et al. Five year results of the prospective randomized controlled prostatic urethral L.I.F.T. study. Can J Urol. 2017;24(3):8802-13.

16	Gupta N., Rogers T., Holland B., et al. Three-year treatment outcomes of water vapor thermal therapy compared to doxazosin, finasteride and combination drug therapy in men with benign prostatic hyperplasia: Cohort data from the MTOPS trial. J Urol. 2018;200(2):405-13
17	Kumar N., Vasudeva P., Kumar A., et al. Prospective randomized comparison of monopolar TURP, bipolar TURP and photoselective vaporization of the prostate in patients with benign prostatic obstruction: 36 months outcome. LUTS. 2018;10(1):17-20.
18	McVary K.T., Rogers T., Roehrborn C.G. Rezum water vapor thermal therapy for lower urinary tract symptoms associated with benign prostatic hyperplasia: 4-year results from randomized controlled study. Urology. 2019;126:171-9
19	McVary K.T., Gittelman M.C., Goldberg K.A., et al. Final 5-year outcomes of the multicenter randomized sham-controlled trial of a water vapor thermal therapy for treatment of moderate to severe lower urinary tract symptoms secondary to benign prostatic hyperplasia. J Urol. 2021;206(3):715-724.
20	Otaola-Arca H., Alvarez-Ardura M., Molina-Escudero R., et al. A prospective randomized study comparing bipolar plasmakinetic transurethral resection of the prostate and monopolar transurethral resection of the prostate for the treatment of Benign Prostatic Hyperplasia: Efficacy, sexual function, quality of life, and complications. Int Braz J Urol. 2021;47(1):131-44.