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TECHNOLOGY REVIEW (MINI-HTA)

REZūM THERAPY FOR MANAGEMENT OF BENIGN PROSTATIC HYPERPLASIA

Malaysian Health Technology Assessment Section (MaHTAS)
Medical Development Division
Ministry of Health Malaysia
005 /2021

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EXECUTIVE SUMMARY

Background

Benign prostatic hyperplasia is a urological condition characterised by enlargement of the prostate gland, which results in bladder outlet obstruction. The obstruction gives rise to voiding symptoms (poor urine stream, straining to urinate, hesitancy, incomplete emptying after urinating, interrupted stream) and storage symptoms (frequency, urgency, nocturia, urge incontinence). The prevalence of BPH is more than 50% at age 60 years old and 90% in men over 85 years old. Similarly, the local prevalence of BPH was reported to be increased 8% per decade from 41.7% for men aged 50 to 59 to 65.4% for men aged 70 or more. Hence, LUTS related to BPH represents a significant socio-economic burden to the public health care system, especially in the ageing population. Management of LUTS comprises conservative approaches (reassurance and advice/ watchful waiting), medical therapies and surgical treatments. An innovative method of minimally invasive surgical treatments (MIST) of the prostate provides a potential treatment option aiming to relieve the symptoms with less perioperative risks and morbidity, as well as less sexual dysfunction. A MIST is a procedure with the potential to be performed on a day case basis, avoiding general anaesthetic boasting a potentially lower side effect profile than invasive treatments. Rezūm is a novel MIST that has gained increasing attention with an appealing outcome using a convective thermal ablation therapy, also known as water vapour thermal therapy (WVTT).

Objective

The objective of this systematic review was to assess the effectiveness, safety, economic and organisational implications of Rezūm therapy for the treatment of LUTS in men with BPH.

Methods

A comprehensive search was conducted on the following databases without any restriction on publication language and publication status. The Ovid interface: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily 1946 to September 28, 2021; Cochrane Library 2021 Issue 8 - Cochrane Database of Systematic Reviews – Cochrane Central Register of Controlled Trials (CENTRAL). Searches were also run in PubMed. Google was used to search for additional web-based materials and information. Additional articles were identified from reviewing the references of retrieved articles. Last search was conducted on 30 September 2021.

Results

A total of 220 titles were identified through the Ovid interface and PubMed, and five were identified from references of retrieved articles. After removing duplicate articles, 105 titles were screened using the inclusion and exclusion criteria. Of these, 23 relevant abstracts were retrieved in full text. After reading, appraising and applying

the inclusion and exclusion criteria, only 15 full text articles were eligible to be included for qualitative synthesis. The 15 selected full text articles comprised one network meta-analysis, one randomised control trial (RCT), three before and after studies, eight cohort studies and two economic evaluation studies.

Effectiveness

Based on limited available evidence, Rezūm therapy had shown to improve urologic symptoms and quality of life as early as six months post procedure and remained durable through five years follow-up. In comparison to medical monotherapy, Rezūm demonstrated more significant improvement in lower urinary tract symptoms and a slower rate of clinical progression among BPH patients. Through an indirect comparison between MIST procedures, Rezūm therapy displayed comparable effectiveness outcomes to UroLift, but was inferior to Aquablation at two years follow-up. The TURP procedure (gold standard) was found to cause a more significant improvement in urologic symptoms and quality of life compared to Rezūm therapy at different time intervals up to two years of follow up periods. Application of Rezūm therapy for large-sized prostates (≥ 80mls) showed comparable improvement with small-sized prostates (<80mls).

Safety

Rezūm therapy was considered safe. Even though the occurrence rate of adverse events was high, most reported adverse events were minor adverse events (CDC I-II) with transient effects. They occurred within 30 days post procedure. Most commonly reported adverse events include dysuria (17%-22%), UTI (11%-17%), urinary retention (4%-34%) and haematuria (11%-18%). Serious adverse events were rare, which include bladder neck contracture, sepsis or severe haematuria requiring return to theatre. Rezūm therapy was associated with minimal sexual dysfunction, contrary to medical treatment and TURP procedure. No de novo erectile dysfunction was reported. The reported retrograde ejaculation (RE) rate was less than 12%. Rezūm therapy had a surgical retreatment rate of 4% at two years follow-up and 4.4% at five years follow-up. However, it was reported to have a higher retreatment rate than TURP (4% versus 1.5% at two years post-procedure). The medical retreatment rate with alpha-blockers following Rezūm therapy at one, two, three, four and five years were 0.7%, 2.2%, 3.7%, 5.2% and 11.1%, respectively.

Cost and Cost-effectiveness

There was no retrievable published local Malaysian price of Rezūm system. Based on the 2016 US Medicare national average fee schedules, the cost of Rezūm therapy (US$2,489) was cheaper compared to TURP (US$4,821) and Urolift (US$6,230). The price of Rezūm therapy included pre-operative assessment with cystoscopy, transrectal ultrasound (TRUS), urodynamic study (UDS), post-operative assessment, and one year follow-up appointment. From the perspective of Irish hospital care, when both Rezūm and TURP procedures were done under general anaesthesia, as inpatient cases, there was a significant cost saving of €1986.52 per patient for Rezūm therapy. An overall up-front cost saving was €22,819 with an additional 19 bed days and five theatre hours spared. If the Rezūm procedure was

performed as a pure daycare case and patients were discharged from the daycare ward, further saving of €623 per Rezūm patient compared to TURP could be achieved. Similarly, economic analyses from the UK healthcare system and American third-party payer's perspective showed that Rezūm therapy was a cost-saving procedure compared to other MISTs and invasive surgeries (HoLEP and TURP).

Organisational

Two international guidelines, namely AUA and NICE guidelines, recommend Rezūm therapy as one of the MIST options for managing LUTS secondary to BPH. It is considered an alternative treatment for men with moderate to severe LUTS with a prostate volume between 30mls and 80mls. Based on retrievable evidence on Rezūm treatment delivery, Rezūm therapy had been shown to have a shorter procedural time and time taken to return pre-operative activity level. The mean duration of postoperative catheterisation was three to five days. Most reported Rezūm procedures were done under oral or IV sedation and prostatic block. The said learning curve for urologists was three cases.

Social

There was a high level of satisfaction with the Rezūm procedure among the patients, either with the experience or the procedure's outcome. Most patients would recommend the procedure to a friend in similar circumstances. However, when a comparison was made with the UroLift procedure, patients seemed to be more satisfied with the experience and the outcome of UroLift treatment.

Conclusion

Rezūm therapy demonstrated the ability to improve urologic symptoms and quality of life, and to slow down the rate of clinical progression among BPH patients. Its effectiveness was comparable to UroLift, but inferior to Aquablation and the gold standard TURP procedure. Application of Rezūm therapy for large sized prostates (80-120mls) showed comparable improvement with small sized prostates (<80mls). Majority of BPH patients who underwent Rezūm therapy experienced transient minor adverse effects, which include dysuria, UTI, urinary retention and haematuria. No *de novo* erectile dysfunction was observed. Lower rate of retrograde ejaculation was reported. Rezūm therapy was shown to be a cost-saving procedure in comparison to other MISTs and invasive BPH surgeries (HoLEP and TURP). The net cost saving was significantly associated with its lower procedural cost (inclusive of preoperative assessment and follow-up visits), reduction in bed days and operation theatre hours spared. Patient's satisfaction level with the experience and outcome of Rezūm therapy was good.

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ABBREVIATION

AE	adverse event
BPH	benign prostatic hyperplasia
BPHII	BPH impact index
ED	erectile dysfunction
HoLEP	holmium nucleation of prostate
ICER	incremental cost-effectiveness ratio
IIEF	international index of erectile function
IPSS	international prostate symptom score
LUTS	lower urinary tract symptoms
MCID	minimal clinically important difference
LOS	length of hospital stay
MSHQ-EjD	men's sexual health questionnaire for ejaculatory dysfunction
PSA	prostate-specific antigen
PV	prostate volume
PVR	post-residual volume
QALY	quality-adjusted life-year
Qmax	maximum urinary flow
QoL	quality of life
RCT	randomised controlled trial
RE	retrograde ejaculation
ROB 2.0	risk of bias 2.0
ROBINS-I	risk of bias in non-randomised studies of interventions
ROBIS	risk of bias in systematic reviews
TRUS	transrectal ultrasound
TUNA	transurethral needle ablation
TUMT	transurethral microwave therapy
TURP	transurethral resection of the prostate
UDS	urodynamic study
U.S.FDA	U.S. Food and Drug Administration
UTI	urinary tract infection
WVTT	water vapour thermal therapy

1.0 BACKGROUND

Globally, 1 in 4 men is affected by bothersome lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH). [1] It is one of the most common morbidities in elderly men. Benign prostatic hyperplasia is a urological condition characterised by enlargement of the prostate gland, which results in bladder outlet obstruction. The obstruction gives rise to voiding symptoms (poor urine stream, straining to urinate, hesitancy, incomplete emptying after urinating, interrupted stream) and storage symptoms (frequency, urgency, nocturia, urge incontinence). [2] The prevalence of BPH is more than 50% at age 60 and 90% in men over 85 years old. [2] Similarly, the local prevalence of BPH was reported to be increased 8% per decade from 41.7% for men aged 50 to 59 to 65.4% for men aged 70 or more. [3] Hence, LUTS related to BPH represents a significant socio-economic burden to the public health care system, especially in the ageing population.

The management paradigm of LUTS is tailored to symptom severity, the burden to daily living and the level of 'bothersome' to the patients. The severity of symptoms is subjectively measured using a self-reported symptom scoring system, International Prostate Symptom Score (IPSS). [4] The symptom severity is also assessed through clinical parameters, which include maximum urinary flow rate (Qmax), post-void residual volume (PVR), prostatic size and bladder pressure studies. [5] Another scoring system that helps assess the LUTS impact on quality of life (QoL) is the Benign Prostatic Hyperplasia Impact Index (BPHII). [6]

Management of LUTS comprises conservative approaches (reassurance and advice/ watchful waiting), medical therapies and surgical treatments. [7] A watchful waiting (non-medical, non-surgical) policy in addition to lifestyle modifications (fluid management, avoidance of caffeine and use of alcohol) and specific changes in behaviour (bladder retraining, double voiding and urethral milking) are suitable for all men demonstrating BPH related LUTS, that do not complain of high levels of bother. Nevertheless, 15% of patients at one and 35% of patients at five years following watchful waiting will worsen LUTS and seek further management. [8] Medical therapy with alpha-blockers, 5-alpha reductase inhibitors (5-ARI) or a combination of both for mild to moderate bothersome LUTS has a therapeutic ceiling effect in terms of its efficacy and the associated adverse effects. [9] Postural hypotension, dizziness, asthenia, and compromised sexual function are the main reasons for discontinuation. [9] Transurethral resection of the prostate (TURP) has been regarded as the gold standard surgical treatment but is not without potential significant morbidity and long-term sequelae. It can achieve retreatment rates of 2.9% after one year, 5.8% after five years, and 7.4% after eight years. [10] However, it is also associated with early postoperative complications such as urinary retention, postoperative bleeding with or without clot retention, and urinary tract infection. Late postoperative complications include urethral strictures (3.8%), bladder neck contractures (4.7%), erectile dysfunction (6.5%), and retrograde ejaculation (65.4%).[11] Furthermore, it requires the use of general or spinal anaesthesia and carries a mean hospital stay of two days. [9] Holmium enucleation of the prostate (HoLEP) is another invasive surgical treatment reserved for larger prostate. [12] It has mostly replaced open prostatectomy. It carries similar risks and benefits as TURP. An innovative approach of minimally

invasive surgical treatments (MIST) of the prostate provides a potential treatment option to relieve the symptoms with less perioperative risks and morbidity than TURP and less sexual dysfunction. [13] They are of interest to men seeking office-based procedures and the ability to preserve ejaculatory function. Figure 1 depicts the history of medical and surgical treatment for BPH.

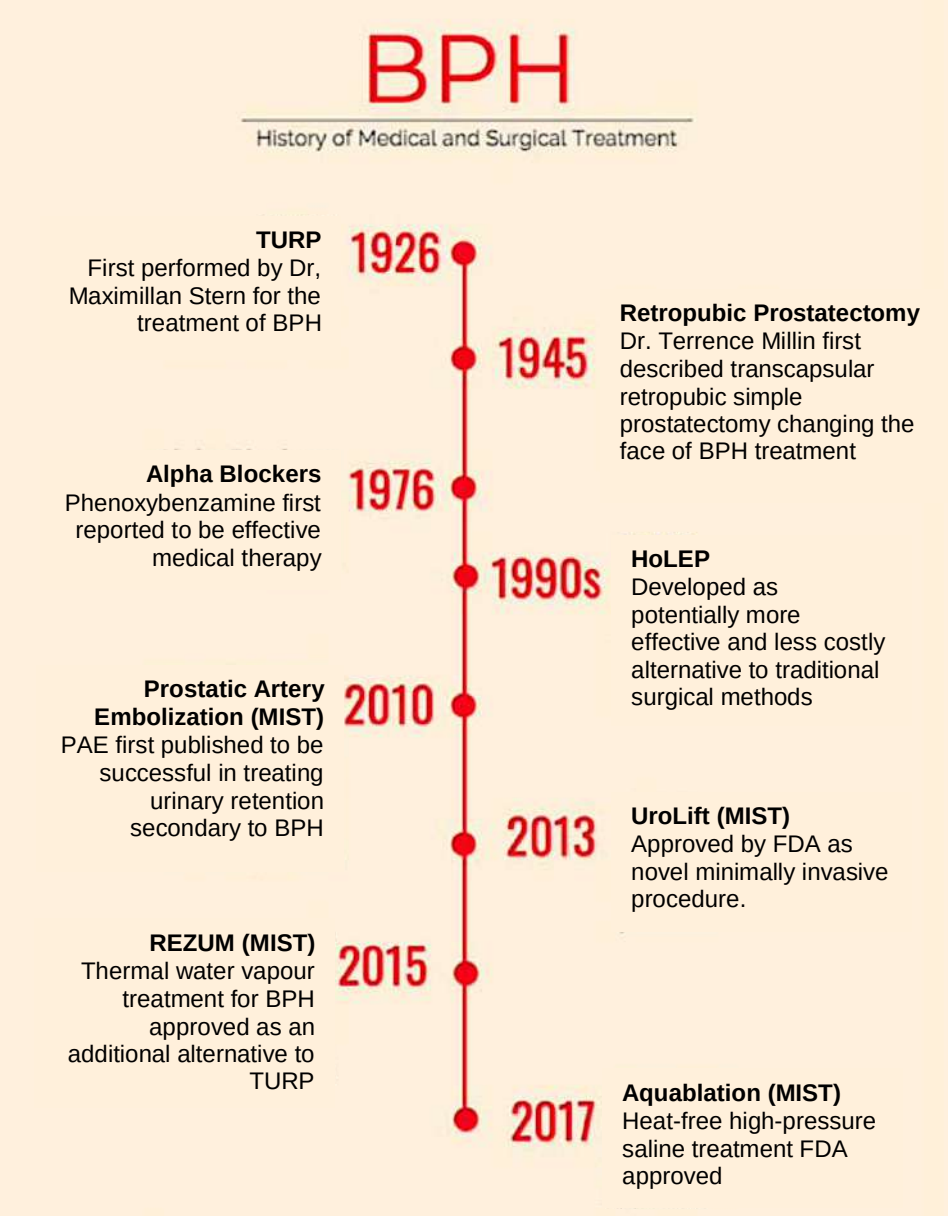

Figure 1: History of medical and surgical treatment for BPH[14]

A MIST is a procedure with the potential to be performed on a day case basis, avoiding general anaesthetic, boasting a potentially lower side effect profile than invasive treatments. Recent choices of these interventions are prostate artery embolisation (PAE), prostatic urethral lift known as UroLift, water jet dissection, AquaBeam system known as Aquablation and Rezūm therapy (Table 1).[12]

Table 1: Three MIST used in the management of LUTS secondary to BPH

	UroLift®	Rezūm	Aquablation
Description	Mechanical displacement of prostate lobes using implants	Water vapour uses convective heating to ablate prostate tissue	High pressure saline hydrodissects the prostate under robotic control
Anaesthesia	Local ± sedation	Local ± sedation ± regional block	General anaesthetic or spinal
Urinary catheterization	Not required	Required for 3–5 days	Removed 1 day post procedure
Guidelines recommendation			
NICE	X	X	In specific circumstances
EAU	X		X
AUA	X	X	X

AUA = American Urological Association; EAU = European Association of Urology; NICE = National Institute for Health and Care Excellence

Rezūm is a novel MIST that has gained increasing attention with an appealing outcome using a convective thermal ablation therapy, also known as water vapour thermal therapy (WVTT). It employs water vapour as a vector for thermal energy, which aims to cause immediate cell necrosis in the prostate without the need for long conduction time or high-energy transfer. To date, Rezūm therapy has not yet been made available in the Ministry of Health hospitals in Malaysia. This technology review was requested by Medical Practice Division, Ministry of Health Malaysia to assess the safety, effectiveness and cost-effectiveness of Rezūm therapy for the management of BPH.

2.0 OBJECTIVE

The objective of this systematic review was to assess the effectiveness, safety, economic and organisational implications of Rezūm therapy for the treatment of LUTS in men with BPH.

3.0 TECHNICAL FEATURE

The Rezūm System

The Rezūm system consists of two components: a portable radiofrequency power supply generator and a single-use transurethral delivery device that incorporates a standard rigid cystoscope lens, which allows the procedure to be performed under direct visualisation (Figure 2). [15] A radiofrequency thermal energy, in the form of water vapour is created to ablate the prostatic tissue, shrinking the enlarged prostates. This convective heat energy is claimed to be more efficient in comparison to historical tissue conductive heat transfer ablation procedures [transurethral needle ablation (TUNA) or transurethral microwave therapy (TUMT)]. A more extended

heating period is required to achieve a therapeutic temperature in the target tissue via conduction versus convection. [16] Furthermore, convective heating limits the thermal effects within the prostate or in the peripheral zone when the transition zone is targeted. Since vapour is wet thermal energy, there will be no charring, desiccation or carbonisation of the treated tissue. [15] A single-use transurethral delivery device with an 18-gauge retractable vapour needle is used to inject steam at a consistent energy dose into the targeted area.

Multiple thermal treatments are delivered with the retractable vapour needle. The vapour needle is located within the delivery device's insulated lumen until it is deployed into the prostate tissue. The length of the needle that exits the shaft and penetrates the prostate is 10.25 mm in size. The needle is flexible braided silicone tubing with 12 small emitter holes spaced around its tip at 120° intervals to allow a controlled, uniform circumferential dispersion of water vapour into the prostate tissue to create an approximate 1.5 cm-2 cm lesion. [13, 15] (Figure 3)

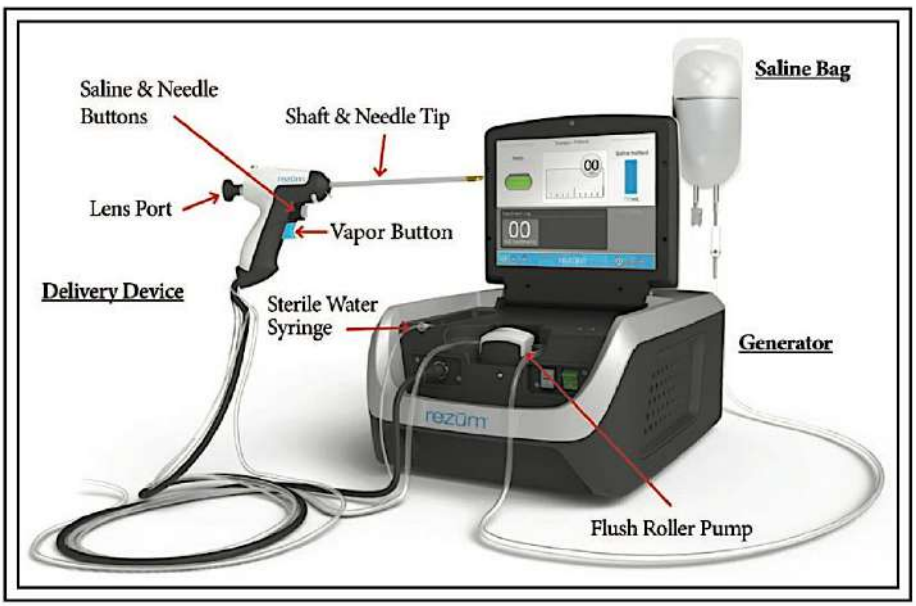

Figure 2: The Rezūm system. Source from Boston Scientific Company, Inc.[15]

Figure 3: Rezūm Delivery Device and Vapour Needle

The Rezūm Procedure [2, 16]

The procedure is visualised using an integrated cystoscope with a standard 4 mm 30° lens. The patient is positioned in the dorsal lithotomy position. (Figure 4) Ensuring a good lithotomy position with the buttocks just off the edge of the table and a clear area beneath the table of any obstruction allows for optimal device movement and delivery of the vapour therapy. A cystoscopic examination is performed to assess the prostatic contour and plan the distribution of thermal lesions. It potentially also provides an opportunity to evaluate the patient's tolerance to rigid cystoscopy while awake. Obtaining an ultrasound scan to assess prostate volume is also helpful.

The treatment needle is initially positioned approximately 1 cm distal from the bladder neck at 3 and 9 o'clock positions. The care provider targets the transition and central prostate adenoma by eye. Each injection deploys 0.5 ml of steam over **nine seconds** at 103 °C raising the tissue temperature to 70 °C. It is recommended to wait an additional one to two seconds after completing the 9-second vapour injection to allow for complete phase change and no loss of vapour through the treatment puncture. After each injection, the needle is retracted, returning to midline and reinserted 1 cm distal to the previous injection until the proximal edge of the verumontanum, creating tissue ablation along the prostate urethra. With each vapour injection, the bulk of the targeted tissue should be treated. For majority of cases, this pattern of treatment produces a smooth case with optimal outcome. All treatments on one side of the gland should be completed first before proceed to treat the contralateral tissue in order to take advantage of the latent heat from prior treatments on the same side. (Figure 5) The total number of injections in each lobe of the prostate is determined by the length of the prostatic urethra and the configuration of the prostate gland. Bole R et al. reported that the maximum number of possible injections was **15 injections** over 135 seconds.[17] During the procedure, continuous saline irrigation (at room temperature) enhances visualization and cools the urethral surface to preserve the urethral lining.

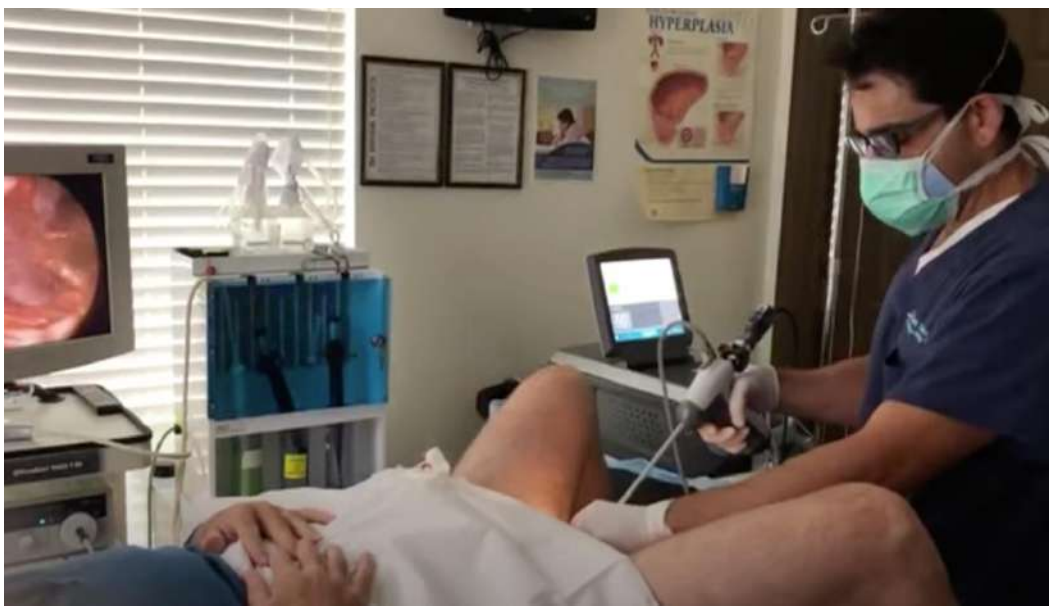

Figure 4: Positioning during Rezūm therapy

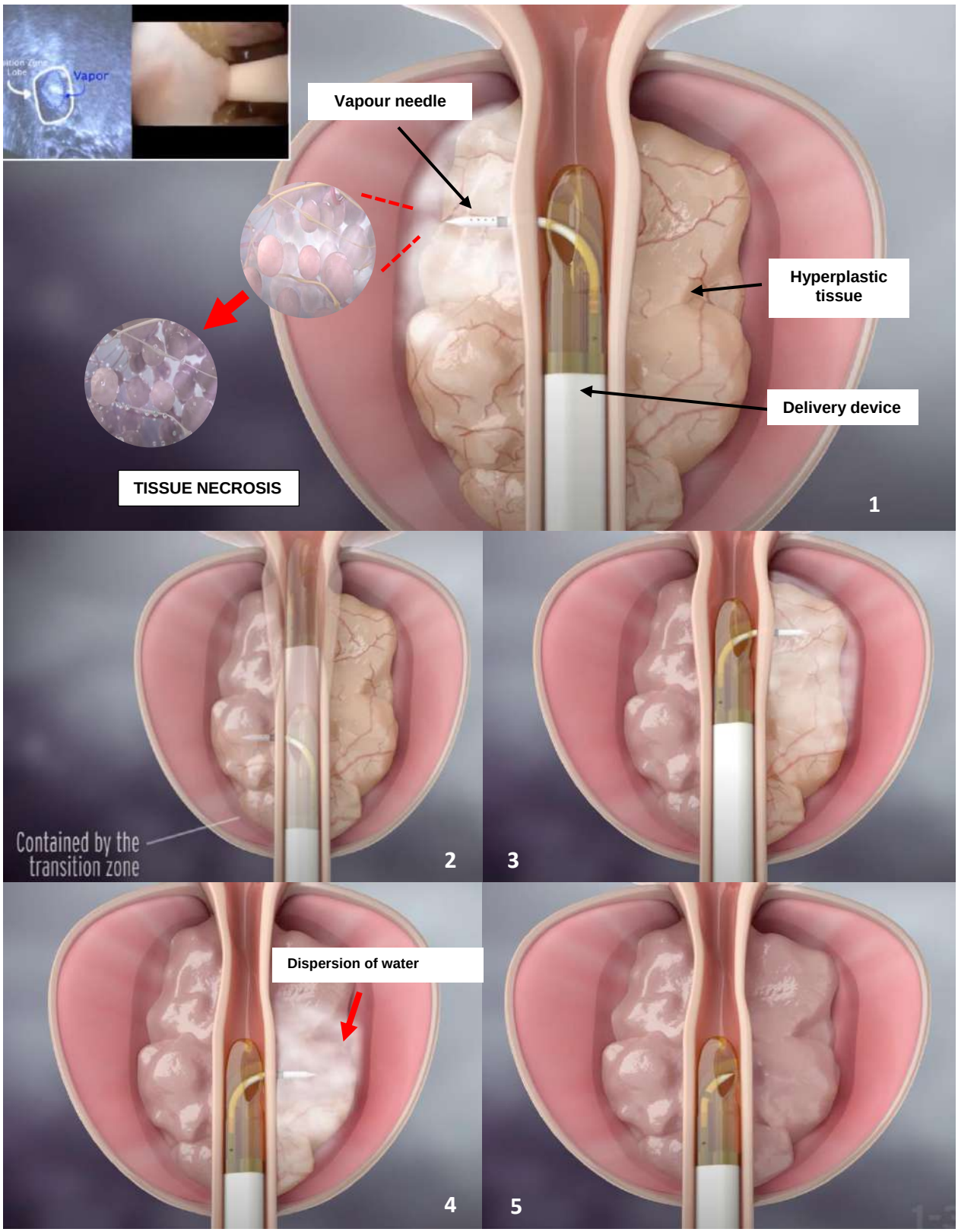

Figure 5: Deployment of vapour needle and thermal treatment

Setting of the procedure

The Rezūm thermal therapy procedure is well suited to be performed in an office or ambulatory outpatient treatment setting with management of discomfort/pain and anxiety based on shared decision making between the patient and urologist.[18]

Pain management and sedation requirement

Studies in the literature have demonstrated that Rezūm therapy can be delivered without a need for general anaesthesia in most cases. Anaesthesia and sedation use is varied and used at the discretion of the urologists. Table 1 shows pain management and sedative options available for Rezūm procedure.[15]

Table 2: Pain management and sedative options for Rezūm procedures [2]

1. Oral Medications
▪ Anti-anxiety i.e., 1-2 mg Alprazolam ▪ Analgesia i.e., 5-10mg hydrocodone/acetaminophen 5-10mg oxycodone/acetaminophen ▪ Anti-inflammatory i.e., ibuprofen
2. Local Nerve Block
▪ Periprostatic nerve block technique Suggested pain management option: belladonna and opium 16.2mg/30mg suppository at the time of prostate block
3. IV Sedation
IV sedation as per institution anaesthesia protocol i.e., IV propofol with monitored office anaesthesia

Patient selection [19]

Patients with BPH are not necessarily the suitable candidates for Rezūm therapy (Table 3). However, in contrast with some other procedures, patients with median lobe obstruction are eligible to receive Rezūm therapy. In many published studies, factors that preclude patients from receiving Rezūm therapy include previous surgical/radiation treatment involving the prostate, a history of urinary retention and patients with a large prostate burden (>120 mls).

Table 3: Selection criteria used in most Rezūm studies

Inclusion criteria	Exclusion criteria
▪ >45 years with symptomatic BPH ▪ IPSS 13 or greater ▪ Qmax between 5mls and 15mls per second ▪ Prostate volume <120 mls	▪ Prior invasive prostate intervention/surgery ▪ PVR > 300mls ▪ PSA > 2.5 ng/ml ▪ Recurrent/active urinary tract infection

IPSS, International Prostate Symptom Score; PVR, post-residual volume; PSA, prostate-specific antigen.

4.0 METHODS

4.1 SEARCHING

A comprehensive search was conducted on the following databases without any restriction on publication language and publication status. The Ovid interface: Ovid

MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily 1946 to September 28, 2021; Cochrane Library 2021 Issue 8 - Cochrane Database of Systematic Reviews – Cochrane Central Register of Controlled Trials (CENTRAL). Searches were also run in PubMed. Google was used to search for additional web-based materials and information. Additional articles were identified from reviewing the references of retrieved articles. Last search was conducted on 30 September 2021.

Appendix 1 showed the detailed search strategies.

4.2 SELECTION

A reviewer screened the titles and abstracts against the inclusion and exclusion criteria and then evaluated the selected full text articles for final article selection.
The selection of articles was done by one reviewer and reviewed by another reviewer.

The inclusion and exclusion criteria were:

Inclusion criteria

Population/ Problem	Men with benign prostatic hyperplasia (BPH) experiencing moderate-to-severe lower urinary tract symptoms (LUTS)
Interventions	Rezūm therapy (convective radiofrequency water vapour thermal therapy/ convective thermal ablative therapy)
Comparators	i. No comparator/sham procedure (as control with no active intervention)/ ii. Transurethral resection of the prostate (TURP)/ simple prostatectomy/laser ablations/laser enucleations/other minimally invasive therapies/ iii. Lifestyle changes and watchful waiting/ iv. Drug therapies
Outcomes	**i.** Efficacy: improvement or resolution in urologic symptoms and quality of life **ii.** Safety: adverse events or procedure-related complications • Device-related adverse events. • Rate of dysuria (pain) • Rate of persistent LUTS (poor stream, frequency) • Rate of urinary retention • Rate of requirement of subsequent surgical re- intervention **iii.** Economic implication (cost, cost-effectiveness) **iv.** Organisational issues
Study design	Health Technology Assessment (HTA), Systematic Review, Meta-analysis Randomised Controlled Trial (RCT), Non-randomised trial, cohort, case-control, cross-sectional and economic evaluation studies.
	English full text articles

Exclusion criteria

Study design	Studies conducted in animals, case series or case reports
	Non English full text articles

Relevant articles were critically appraised using The Cochrane Collaboration's tools. All full text articles were graded according to US/Canadian Preventive Services Task Force (Appendix 2). Data were extracted and summarised in evidence table as in Appendix 4.

5.0 RESULTS

A total of 220 titles were identified through the Ovid interface and PubMed, and five were identified from references of retrieved articles. After removal of duplicate articles, 105 titles were screened using the inclusion and exclusion criteria. Of these, 23 relevant abstracts were retrieved in full text. After reading, appraising and applying the inclusion and exclusion criteria, only 17 full text articles were eligible to be included for qualitative synthesis. The 17 selected full text articles comprised of one network meta-analysis, one randomised control trial (RCT), three before and after studies, eight cohort studies and four economic evaluation studies. The selection of studies is as shown on Figure 5.

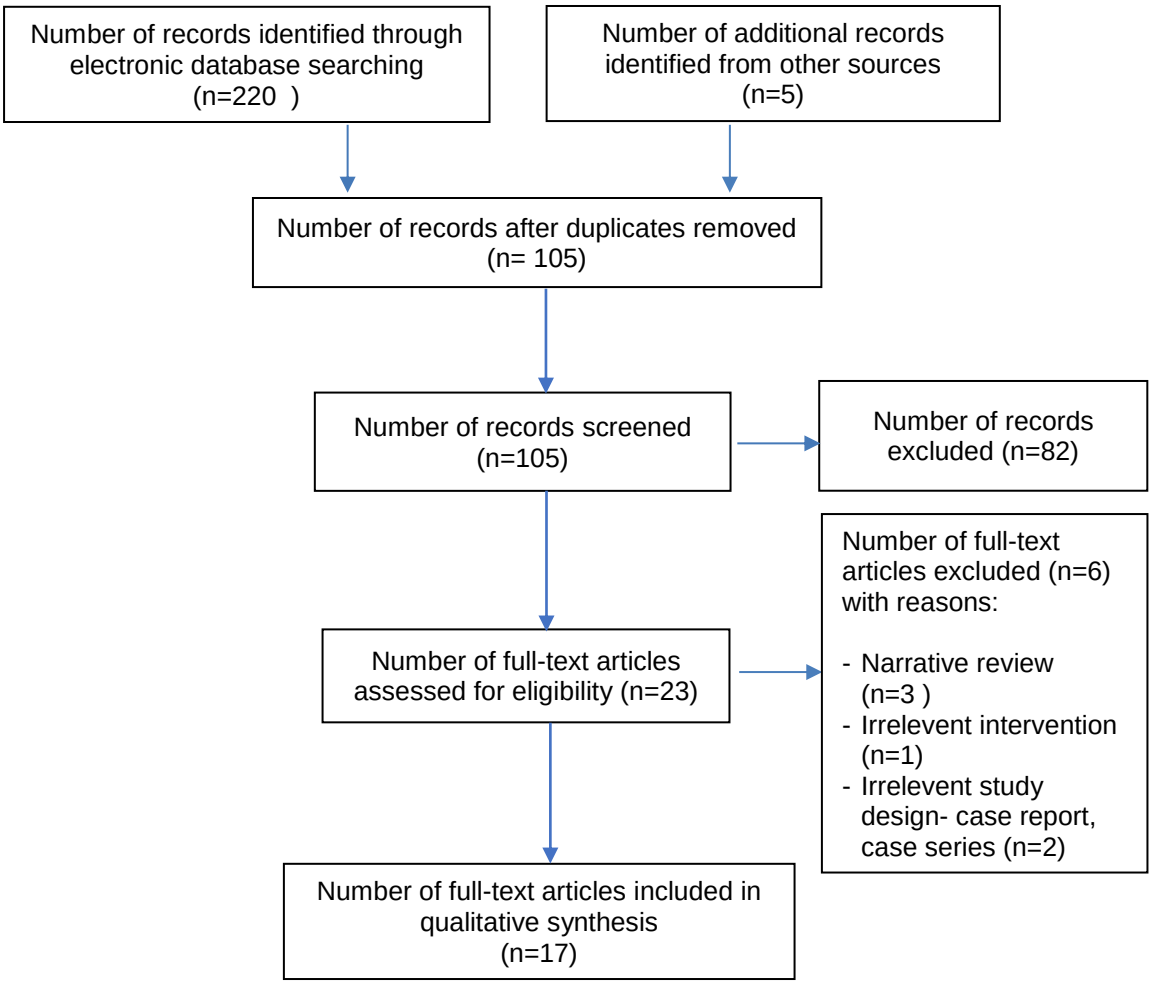

Figure 5: Flow chart of study selection

Assessment of risk of bias in included studies

Risk of bias was assessed using Risk of Bias in Systematic reviews (ROBIS) for systematic review and meta-analysis, Cochrane Risk of Bias (ROB) 2.0 for RCT, and Cochrane Risk of Bias In Non-randomised Studies of Interventions (ROBINS-I) for observational studies. These assessments involved answering a pre-specified question of those criteria assessed and assigning a judgement relating to the risk of bias.

Risk of bias assessment for included systematic review and meta-analysis

Tanneru K et al. was rated to have an overall low risk of bias. The review had pre-specified its clinical question and inclusion criteria for study eligibility. No language restriction was applied. There was some concern regarding the method used to identify and select the studies. While the search terms were mentioned in the article, the full search strategy was not reported. However, the inclusion assessment, appraisal and data collection process were reported to have been conducted independently by at least two reviewers. The quantitative synthesis (network meta-analysis) undertaken was considered appropriate. No detail was provided on statistical heterogeneity. The authors also did not state whether sensitivity analyses were used to assess the robustness of their findings. However, the included studies were reported to have comparative patients' demographic and baseline data.

Table 3: Summary of risk of bias assessment for systematic review and meta-analysis using ROBIS

REVIEW	D1	D2	D3	D4	OVERALL
Tanneru K et al.[11]	+	-	+	-	+

Domains
D1: Study eligibility
D2: Identification and selection of studies
D3: Data collection and study appraisal
D4: Synthesis and findings

Judgement
X High risk
\- Unclear
\+ Low risk

Risk of bias assessment for included RCT

McVary et al. was rated to have an overall low risk of bias. Random sequence generation and allocation concealment were performed adequately. There was some concern with the blinding process as it was not possible to blind the urologists who performing the treatment procedure or the sham procedure. This could introduce performance bias. Participants were reportedly blinded so there was low risk of bias for subjective measurements (urologic symptom scores, QoL, erectile function, ejaculatory function, minor adverse events). Blinding was considered not relevant for objective measurements (major adverse events, retreatment, acute urinary retention). Outcomes were analysed using intention to treat analysis. Nevertheless, the sexual function outcomes (erectile function and ejaculatory function) were measured in a limited subset of participants who were sexually active at baseline

and during the follow-up period. Selective reporting was considered to have a low risk of bias as all prespecified outcomes were reported and analysed. Since the study was sponsored by device manufacturer, funding could be a source of bias. It could lead to overestimation of benefits or underestimation of harms of Rezūm therapy.

Table 4: Summary of risk of bias assessment for RCT using ROB 2.0

REVIEW	D1	D2	D3	D4	D5	OVERALL
McVary et al.[20]	+	-	-	+	+	+

Domains
D1: Bias arising from the randomisation process
D2: Bias due to deviations from intended intervention
D3: Bias due to missing outcome data
D4: Bias in measurement of the outcome
D5: Bias in selection of the reported result

Judgement
High risk
Some concern
Low risk
No information

Risk of bias assessment for included cohort studies

The effect of interest for this assessment was pre-specified as the effect of assignment of the interventions at baseline because this will most closely resemble how Rezūm therapy would be performed in typical urologic practice. Time-varying confounding had not been considered as it was not relevant in this setting. In assessing bias due to confounding, factors namely age, prostate size, baseline subjective and objective measurements of outcome variables, BPH medication usage and comorbidities were considered as source of baseline confounding in the context of this review. Six studies[17, 21-25] had serious risk of bias due to baseline confounding. Even though baseline characteristics were presented, it was unclear whether the authors had considered all the important prespecified confounders (age, prostate size, baseline LUTS severity scoring), or if the analyses were conducted specifically to investigate the confounding effects. Based on the literature, age is a known risk factor in BPH surgery, with increased risk of postoperative complications among older men.[26, 27] While prostate volume and baseline LUTS severity score significantly influence outcomes and complications of MIST procedure, and patient global ratings of improvement, respectively.[28] None of these studies reported any statistical adjustment made to control the confounding. One study [29] was rated moderate risk as it attempted to control for most of the important baseline confounders with pre-specified eligibility criteria. One study [30] was rated low risk of bias as the authors conducted propensity matching to ensure comparable groups at baseline and all baseline confounders were considered. Bias due to selection of participants among the included studies was rated ranging from low to serious risk of bias. Mollengarden et al.[22] had serious risk of bias for selecting participants into their study as it was based on clinical judgement of the urologist. Six studies were rated as being at moderate risk of bias, mainly due to limited information on selection of participants and the retrospective design (lead time bias). All studies were rated low risk of bias in classification of intervention for Rezūm therapy and bias due to deviations from intended interventions as the intervention was clearly defined, whereby misclassification of intervention status would be unlikely and all participants received the intended intervention. When assessing bias due to missing data, five

studies[17, 21, 22, 24, 25] were at serious risk of bias from missing baseline data and data for assessed outcomes. Three studies were rated low risk of bias whereby in two studies[23, 29], the data were reasonably complete and one study[30] utilised post hoc analysis to adjust for missing longitudinal data. Given that in all included observational studies, blinding of the participants was not done, these studies were rated to be at moderate risk of bias due to measurement of outcomes. Lack of blinding might have influenced some participant- reported or subjectively assessed outcomes, contributing to bias due to selective recall and delays in the recall period. Some of the outcomes (Qmax, PVR, PSA) were measured objectively, hence remain unaffected. The risk of bias in selection of the reported result was considered low in all studies, as all prespecified outcomes were reported and analysed. The overall judgement on risk of bias for each observational study rated six studies.[17, 21-25] with serious risk of bias and two studies with moderate risk of bias[25, 29].

Table 5: Summary of risk of bias assessment for observational studies using ROBINS-I

REVIEW	D1	D2	D3	D4	D5	D6	D7	OVERALL
Tutrone et al.[21]	X	-	+	+	X	-	+	X
Mollengarden et al.[22]	X	X	+	+	X	-	+	X
Sienna et al.[29]	-	+	+	+	+	-	+	-
Johnston et al.[23]	X	-	+	+	+	-	+	X
Darson et al.[24]	X	-	+	+	X	-	+	X
Gupta N et al.[30]	+	-	+	+	+	-	+	-
Bole R[17]	X	-	+	+	X	-	+	X
Garden EB[25]	X	-	+	+	X	-	+	X

Judgement
D1: Bias due to confounding
D2: Bias due to selection of participants
D3: Bias in classification of interventions
D4: Bias due to deviations from intended interventions
D5: Bias due to missing data
D6: Bias in measurement of outcomes
D7: Bias in selection of the reported result

Domains
Critical risk
Serious risk
Moderate risk
Low risk
No information

Characteristics of included studies

One network meta-analysis[11] and 13 primary studies[17, 21-25, 29-37] reported on the effectiveness of Rezūm therapy. Sixty-four percent of these studies was published within the last two years. The network meta-analysis comprised of four randomised control trials [Rezum (one study); UroLift (two studies); Aquablation (one study)]. Sham procedure was used as the control group in two studies and TURP in the other two studies. Table 6 displays the characteristics of included primary studies. Among the primary studies, eight studies were single-arm studies (without comparator), one study compared Rezūm therapy with sham procedure (rigid cystoscopy with simulated active treatment sound effects)[35-37], one study had UroLift as comparator[21] and one study compared Rezūm therapy with medical treatment[30]. Two studies investigated the feasibility of Rezūm therapy in larger prostate size (>80mls).[17, 25] Eight studies were conducted in multi-centre setting. [21, 24, 29, 30, 32-37] Majority of the studies were conducted in United State. [17, 21, 22, 24, 25, 30, 34-37] Other study locations include Ireland[31], Italy[29], France[32], United Kingdom[23], Dominican Republic[33], Czech Republic[33] and Sweden[33]. Six studies[21, 24, 30, 33-37] received funding from industry to conduct their studies. One study[21] was sponsored by NeoTract/Teleflex, Inc. and five studies were sponsored by NxThera, Inc., Maple Grove, MN, USA[24, 30, 33-37]. A study by Dixon et al.[33] was a proof of concept study, while Darson et al. conducted a post marketing study[24]. A pivotal study by McVary et al. has been the only RCT conducted to assess Rezūm therapy so far. It involved 15 study sites in the USA and has the longest follow-up period (five years). The authors have produced five publications[20, 35-38] of the effectiveness findings within the five years period of the study. A publication by Roehrborn et al[34] reported the result of crossover arm of McVary et al. trial. Gupta N et al.[30] utilised data from two RCTs [McVary Rezūm II trial [20-22] and MTOP trial [39, 40] (both were NxThera, Inc., sponsored studies)] to conduct a comparative study between Rezūm therapy and medical treatment for BPH. The number of participants in the included primary studies ranged from ten to 1275. The mean age of participants ranged between 62.4(±7.3) and 72 (±10) years old. The mean prostate volumes ranged from 44.5(±13.3)mls to 72.0(±35.0)mls. In studies comparing the effectiveness of Rezūm therapy among small prostates and large prostates, the large prostates cohort had mean prostate volumes from 106.8 (±37.6) mls to 119 (±26) mls.[17, 25] Participants were follow up for two months to five years period.

Table 6: Characteristics of included primary studies

First author (publication year)	Study design	Study location	Industry funding	Comparator	Sample size	Mean age (± SD) (years)	Mean baseline prostate size (± SD) mls	Follow-up duration
Tutrone[21] (2020)	Prospective cohort	USA (2 sites)	Yes	UroLift	53 (Rezum group-23)	69(8.6)	56 (30.1) Rezum - 63 (30.9) Urolift - 49 (28.4)	2 months
Haroon[31] (2021)	Before and after study	Ireland (single site)	No	-	10	70(9.3)	72.0 (35.0)	3 months
Mollengarden[22] (2018)	Retrospective cohort	USA (single centre)	No	-	129	67.8(8.0)	52.6 (17.0)	6 months
Sienna[26] (2021)	Prospective cohort	Italy (5 sites)	No	-	135	* 69 (61-79)	*60 (45–78)	6 months
Alegorides C[29] (2020)	Before and after study	France (2 sites)	No	-	62	64.3 (11.9)	54.3 (28.4)	1 year
Johnston[23] (2020)	Prospective cohort	UK (single centre)	No	-	210	66(NR)	56.9 (NR)	1 year
Darson[24] (2017)	Retrospective cohort	USA (2 sites)	Yes	-	131	70.9(9.4)	45.1 (23.4)	1 year
Dixon[30] (2015)	Before and after study – pilot study	Dominican Republic, Czech Republic, Sweden (3 sites)	Yes	-	65	66.6(7.7)	48.6 (20.5)	2 years
Roehrborn[31] (2017)	Before and after study (participants from crossover arm of McVary[18] study)	USA (15 sites)	Yes	-	53	63.8(7.3)	44.5 (13.3)	2 years

First author (publication year)	Study design	Study location	Industry funding	Comparator	Sample size	Mean age (± SD) (years)		Mean baseline prostate size (± SD) mls		Follow-up duration
Gupta N[27] (2018)	Retrospective cohort study (Data drawn from 2 large RCTs)	USA (Rezum group-15 sites; medical therapy group-17 sites)	Yes	Medical therapy (Doxazosin/ Finasteride/ combination)	1275 (Rezum-129/ Doxazosin-368/ Finasteride-394/ Combo-384) *(propensity matching)*	*Mean age range* [62.4(7.3)-63.3(7.0]		Rezum -46.0(13.1) Doxazosin - 39.3 (10.1) Finasteride - 38.0 (8.9) Combo – 37.7(9.5)		3 years
McVary[20, 32-34] (2021)	RCT (pivotal study)	USA (15 sites)	Yes	Sham control (rigid cystoscopy with simulated active treatment sound effects)	197 (Rezum group-135)	63(7.1)		45.8 (13.0)		5 years
Large prostates (≥ 80mls) studies										
Bole R[17] (2020)	Retrospective cohort study	USA (single centre)	No	Large prostate (LP) vs small prostate (SP)	182 LP-47 SP-135	**LP** 72 (10)	**SP** 69 (9)	**LP** 119 (26)	**SP** 49 (18)	3 months
Garden EB[25] (2021)	Retrospective cohort study	USA (single centre)	No	LP vs SP	204 LP-36 SP-168	**LP** 67.3 (7.2)	**SP** 65.4 (9.1)	**LP** 106.8 (37.6)	**SP** 45.3(14.5)	1 year

5.1 EFFECTIVENESS

5.1.1 Patient reported outcome measures

International Prostate Symptom Score (IPSS)

The International Prostate Symptom Score (IPSS) is a validated questionnaire used to assess symptoms of BPH. It includes seven dimensions with 5-point rating scale (incomplete bladder emptying, frequency, intermittency, urgency, weak stream, straining and nocturia).[4] Higher scores represent worse symptoms [IPSS score < 8 (**mild LUTS)**; IPSS score between 8 and 19 (**moderate LUTS**); IPSS score ≥ 20 (**severe LUTS**)].[41] A decrease in IPSS is indicative of symptom improvement. An improvement in the IPSS score by three points for mild LUTS, five points for moderate LUTS and eight points for severe LUTS are considered to be the minimal clinically important difference (MCID) to assess efficacy and comparative effectiveness.[42] Ten included studies reported on the improvement of IPSS score from baseline (Table 7). The participants had moderate to severe LUTS at baseline, which reflected by the mean baseline IPSS score [range: 18.0(6.6) - 22.0 (4.8)]. The maximum improvement in IPSS score [mean changes range: - 10.0(7.9) to -13.9(7.9)] was reached at six months with 47%- 68% reduction in LUTS symptoms.

Table 7: Mean changes in IPSS score from baseline at different follow-up intervals

STUDY	Mean IPSS Score (± SD) [Change in mean IPSS Score ± SD] [% change in mean IPSS Score]							
	Baseline	Follow-Up Interval						
		1 month	3 months	6 months	1 year	2 years	3 years	4 years	5 years
Tutrone[21]	18.0(6.6)	15.6(9.2) [-6.0] NR							
Haroon[31]	20.8 (4.0)	NR NR NR	5.3 (1.5) [-15.5(2.5)] [74.5%]						
Mollengarden[22]	18.5 (7.4)	11.2 (6.4) [-7.3(8.8)] [26.1%]	8.5 (5.9) [10.1(7.7)] [50.2%]	6.9 (5.0) [-11.6(7.0)] [60.0%]					
Sienna[29] *	21.5(17-25)	7.5(5-12) NR	4.2(3.2-5.3) NR	4.4(3.8-5.9) NR					
Alegorides C[32]	20.0 (6.3)	10.3 (5.7) [−9.7(8.4)] [48.5%]	7.9 (5.0) [−11.6(8.7)] [59.5%]	6.5 (4.2) [−13.9(7.9)] [68.1%]	7.5 (4.7) [−12(8.7)] [61.5%]				
Roehrborn[34]	20.0 (6.6)	15.3 (8.3) [-4.7(10.5)] [0.7%]	9.8 (6.0) [-10.0(7.1)] [47.0%]	10.2(6.9) [-10.0(7.9)] [47.0%]	8.6 (6.6) [-10.8(8.1)] [47.0%]				
Johnston[23]	20.4	NR NR	5.9 NR	5.5 NR	4.3 NR				
Darson[24]	19.5 (6.6)	16.0 (8.0) [-3.9(8.2)] [15.9%]	9.8 (6.9) [-10.1(8.8)] [47.2%]		10.1(7.2) [-9.4(8.7)] [45.2%]				
Dixon[33]	21.6 (5.5)	14.8 (8.4) [-6.8(10.0)] NR	8.3 (5.8) [-13.4(7.6)] NR	8.5 (7.0) [-13.1(8.6)] NR	9.2 (6.5) [-12.5(7.6)] [56.0%]	9.6 (6.5) [-12.1(7.9)] [55.0%]			
McVary[20, 35-37]	22.0 (4.8)	NR NR NR	10.6 (6.4) [-11.3(7.6)] [50.0%]	9.8 (6.2) [-12.2(7.6)] [54.0%]	10.3 (6.7) [-11.6(7.3)] [52.2%]	10.2 (6.2) [-11.2(7.3)] [50.7%]	10.5(6.1) [-11.0(7.0)] [49.7%]	11.4(7.4) [-10.1(7.6] [46.7%]	11.1(7.8) NR [48.0%]

*IPSS reported in median (IQR); NR = not reported

IPSS-QoL Score

The IPSS-QoL score is question 8 of the IPPS, which states "If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?".[4] Scores range from 0 (delighted) to 6 (terrible), thus a lower score indicates patient benefit. No threshold has been established for the IPSS-QoL to indicate MCID. However, a Cochrane review on Rezūm therapy had considered MCID of -0.5 to assess efficacy and comparative effectiveness.[28] This outcome was reported in seven studies, which demonstrated an improvement in quality of life (Table 8). Mean changes in QoL score at six months ranged from 43% to 76% in between studies. McVary et al. revealed at the five year follow-up of their RCT that the QoL score trend had plateaued and remained more or less similar since the one year follow-up assessment.

Table 8: Mean changes in IPSS-QoL score from baseline at different follow-up intervals

STUDY	Mean IPSS-QoL Score (± SD) [Change in mean IPSS-QoL Score (± SD)] [% change in mean IPSS-QoL Score]							
	Baseline	Follow-Up Interval						
		1 month	3 months	6 months	1 year	2 years	3 years	4 years	5 years
Haroon[31]	4.4(0.7)	NR NR NR	0.6(0.7) [-3.8] [86.4%]						
Alegorides C[32]	4.5 (1.0)	2.1 (1.6) [−2.5(1.7)] [54%]	1.5 (1.6) [−3.0 (1.8)] [66%]	1.1(1.4) [−3.5(1.6)] [76%]	1.2 (1.6) [−3.2(1.7)] [72%]				
Roehrborn[34]	4.0(1.4)	3.3(1.7) [-0.7(2.0)] [7.0%]	1.9(1.4) [-2.0(1.8)] [45.0%]	2.0(1.4) [-2.0(1.7)] [45.0%]	1.7(1.2) [-2.0(1.6)] [52.0%]				
Johnston[23]	4.3	NR NR	1.4 NR	1.3 NR	1.2 NR				
Darson[24]	4.3(1.2)	3.7(1.8) [-0.6(1.9)] [7.2%]	2.3(1.5) [-2.0(1.7)] [42.7%]		2.5(1.4) [-1.9(1.8)] [37.8%]				
Dixon[33]	4.3(1.1)	2.9(1.8) [-1.5(2.0)] NR	1.5(1.4) [-2.8(1.6)] NR	1.6(1.8) [-2.7(2.0)] NR	1.7(1.4) [-2.7(1.6)] NR	1.8(1.4) [-2.6(1.7)] NR			
McVary[20, 35-37]	4.4(1.1)	NR NR NR	2.3(1.5) [-2.1(1.6)] [46.0%]	2.1(1.5) [-2.3(1.6)] [51.0%]	2.1(1.5) [-2.2(1.6)] [50.1%]	2.1(1.4) [-2.2(1.5)] [49.9%]	2.1(1.3) [-2.2(1.6)] [48.5%]	2.3(1.5) [-2.0(1.7)] [42.9%]	2.2(1.4) NR [45%]

NR = not reported

Benign Prostatic Hyperplasia Impact Index (BPHII)

The Benign Prostatic Hyperplasia Impact Index (BPHII) is a validated self-administered questionnaire used to assess the impact on quality of life caused by urinary symptoms in men with BPH. The impact was assessed in four key domains namely physical discomfort, worry about health, bother and impact on usual activities.[6] The BPHII yields a total score for all four items, ranging from 0 to 13. Lower scores indicate less patient symptoms. A different in score of -0.5 is considered as MCID to assess efficacy and comparative effectiveness [42] The findings from three studies displayed similar improvement trend as IPSS-QoL scores (Table 9).

Table 9: Mean changes in BPHII score from baseline at different follow-up intervals

STUDY	Mean BPHII (± SD) [Change in mean BPHII (± SD)] [% change in mean BPHII]							
	Baseline	Follow-Up Interval						
		1 month	3 months	6 months	1 year	2 years	3 years	4 years	5 years
Roehrborn[34]	5.5(3.3)	NR	2.6(2.6)	2.3(2.5)	1.6(2.3)				
		NR	[-2.9(3.3)]	[-3.3(3.2)]	[-3.6(3.0)]				
		NR	[39.0%]	[57.0%]	[71.0%]				
Dixon[33]	6.8(2.8)	5.5(3.6)	2.2(2.4)	2.0(2.6)	2.0(2.3)	2.3(2.5)			
		[-1.2(4.4)]	[-4.7(3.2)]	[-4.8(3.7)]	[-4.9(3.0)]	[-4.8(3.5)]			
		NR	NR	NR	NR	NR			
McVary[20, 35-37]	6.3(2.8)	NR	2.9(2.9)	2.2(2.6)	2.3(3.0)	2.3(2.7)	2.4(2.8)	2.6(2.9)	2.8(3.2)
		NR	[-3.4(3.5)]	[-4.1(3.0)]	[-3.9(3.3)]	[-3.8(3.1)]	[-3.7(3.3)]	[-3.5(3.4)]	NR
		NR	[46.0%]	[65.0%]	[60.5%]	[61.1%]	[57.3%]	[52.2%]	[48.0%]

NR = not reported

5.1.2 Clinical outcomes

Maximum flow rate (Qmax)

The maximum flow rate (Qmax) is a uroflowmetry measure, with lower values indicating possible bladder outlet obstruction. A Qmax values below 10 mL/s indicate abnormal urinary flow, values between 10 to 15 mL/s are borderline, and values greater than 15mL/s indicate normal urinary flow. The MCID for change from baseline is defined as 2mL/s for Qmax.[43] Qmax was measured in eight included studies. The Qmax values showed incremental improvements from baseline till one year post procedure. McVary et al. reported a sustained improvement (49%) at 5 years follow-up. The finding supported temporal improvement seen with IPSS score.

Table 10: Mean changes in Qmax from baseline at different follow-up intervals

STUDY	Mean Qmax (± SD) , mL/sec [Change in mean Qmax (± SD)] [% change in mean Qmax]								
	Baseline	Follow-Up Interval							
		1 month	3 months	6 months	1 year	2 years	3 years	4 years	5 years
Haroon[31]	9.3(2.5)	NR	13.3(2.3)						
		NR	[4.1(0.2)]						
		NR	[44.1%]						
Mollengarden[22]	10.5(4.3)	13.2(5.0)	16.3(8.6)	16.8(6.9)					
		[3.2(5.0)]	[6.0(8.8)]	[5.9(7.3)]					
		(40.5%)	(71.5%)	(71.7%)					
Alegorides C[32]	11.0(3.4)	13.2(5.1)	14.5(4.8)	16.4(5.1)	16.2(5.3)				
		[2.4(4.9)]	[3.7(5.4)]	[5.7(5.3)]	[6(4.8)]				
		[23.8%]	[31.8%]	[53.2%]	[58.8%]				
Roehrborn[34]	10.1(3.7)	13.2(6.4)	16.4(7.1)	16.1(7.2)	16.2(7.9)				
		[2.9(6.2)]	[6.3(6.8)]	[6.0(7.5)]	[5.9(7.9)]				
		[34.0%]	[74.0%]	[76.0%]	[68.0%]				
Johnston[23]	9.2	NR	15.8	15.2	18.1				
		NR	NR	NR	NR				
Darson[24]	8.6(4.9)	9.6(5.9)	11.6(7.7)		10.0(5.0)				
		[1.3(5.1)]	[3.0(9.0)]		[1.5(5.9)]				
		[20.9%]	[75.3%]		[51.4%]				
Dixon[33]	7.9(3.2)	9.9(3.9)	12.8(6.4)	12.3(5.3)	12.7(6.3)	12.0(6.2)			
		[2.0(4.5)]	[4.7(6.4)]	[4.3(5.5)]	[4.6(6.4)]	[3.7(6.5)]			
		NR	NR	NR	NR	NR			
McVary[20, 35-37]	10.0(2.2)	NR	16.4(7.3)	15.7(6.3)	15.5(6.7)	14.7(6.1)	13.2(4.8)	13.7(5.7)	14.0(5.4)
		NR	[6.4(7.2)]	[5.7(6.2)]	[5.5(6.4)]	[4.8(6.1)]	[3.5(4.6)]	[4.2(5.7)	NR
		NR	[69.0%]	[62.0%]	[58.5%]	[52.5%]	[39.7%]	[49.5%]	[49%]

NR = not reported

Post-void residual urine volume (PVR)

Post-void residual urine volume (PVR) a measurement of urine retention, is usually estimated with ultrasound. Whilst PVR is an objective measurement, it is subjected to a high degree of intra- and inter-patient variability. [44] Post-void residual urine volume was measured in eight included studies. The studies showed similar pattern of significant reduction in PVR as early as one month (five studies) [22, 24, 32-34] and continued to sustain through three years follow-up (one study) [35-37] (Table 11).

Table 11: Mean changes in PVR from baseline at different follow-up intervals

STUDY	Mean PVR (± SD), mL [Change in mean PVR (± SD)] [% change in mean PVR]								
	Baseline	Follow-Up Interval							
		1 month	3 months	6 months	1 year	2 years	3 years	4 years	5 years
Haroon[31]	197(150)	NR NR	51(22) [-146(128)]						
Mollengarden[22]	101.7(114.4)	82.4(85.9) [-19.3(104.7)]	71.5(87.8) [-32(111.5)]	73.1(91.0) [-34.8(119.7)]]					
Alegorides C[32]	78.9(90)	24.2(23.7) [-54.6(92.5)]	25.5(35.5) [-50.8(82.2)]	24.8 (25.6) [−49.8(76.4)]	16.9 (22.5) [−56.4(89.8)]				
Roehrborn[34]	93.1(77.5)	81.5(75.6) [-11.7(85.1)]	67.3(64.2) [-28.4(99.2)]	67.3(64.9) [-24.3(89.2)]	83.8(80.5) [-17.2(105.3)]				
Johnston[23]	170.9	NR NR	100 NR	96.5 NR	108 NR				
Darson[24]	216.8(286.6)	82.5(144.5) [-127(257.1)]	85.8(167.3) [-158(221.8)]		77.3(122.1) [-159(254.7)]				
Dixon[33]	92.1(77.9)	67.1(64.4) [-25.0(131.1)]	59.6(66.4) [-29.9(78.0)]	65.9(88.5) [-21.4(88.3)]	64.5(72.3) [-27.6(82.9)]	62.8(83.9) [-15.6(93.0)]			
McVary[20, 35-37]	82.4(51.8)	NR NR	71.8(72.2) [-10.6(68.3)]	75.0(81.8) [-8.4(75.8)]	78.6(79.9) [-3.9(82.7)]	84.6(92.0) [-0.3(85.3)]	54.1(61.8) [-28.2(65.8)]	75.2(69.7) [-9.2(72.2)]	NR NR

NR = not reported

5.1.3 Rezūm therapy: Large prostate (≥80mls) versus Small prostate (<80mls)

Two studies[17, 25] documented outcomes of patients with large prostates (≥ 80mls) following Rezūm therapy. Bole R et al. reported three months outcomes while Garden EB et al. offered findings beyond three months follow-up period. Both studies had shown a statistically significant improvements in IPSS, PVR and Qmax for large sized prostates which were comparable with small-sized prostates (Table 12).

Table 12: Mean changes in IPSS, Qmax and PVR from baseline at follow-up between large prostate and small prostates

Outcome variables	Bole et al. (2020)		Garden EB et al. (2021)	
	Large prostate	Small prostate	Large prostate	Small prostate
Mean IPSS (± SD)				
Baseline	22.0(5.3) *p=0.04*	22.1(6.0)*p=0.001*	15.2(5.8) *p=0.29*	16.6(6.8) *p=0.003*
At follow-up	13.4(6.7)	12.1(5.4)	12.5(6.5)	11.2(7.3)
Mean Qmax (± SD), mL/sec				
Baseline	7.7 (3.8) *p=0.002*	9.2 (4.5) *p=0.001*	7.4(5.6) *p=0.04*	9.5(5.1) *p=0.18*
At follow-up	12.7 (8.7)	12.9 (6.8)	14.6(13.3)	10.9(6.4)
Mean PVR (± SD), mls				

Baseline	305(209) *p=0.05*	301(252) *p<0.001*	161(141) *p=0.009*	90(107*) p=0.019*
At follow-up	149(132)	157(135)	81(79)	63(89)

5.1.4 Rezūm versus sham procedure

A double blinded, randomised control trial conducted by McVary et al., aimed to investigate comparative outcomes of Rezūm therapy with sham procedure (rigid cystoscopy with simulated active treatment sounds).[20] At three months, Rezūm therapy showed greater improvement in IPSS score compared to sham [mean reduction of -11.2 (95% confidence interval (CI) -12.5, -9.9) in Rezūm arm versus -4.3 (95% CI -6.1, -2.5) in sham arm] (p <0.0001). There was also a significant improvement in QoL of Rezūm group compared to sham group [mean reduction of IPSS QoL -2.1 (95% CI -2.4, -1.8) in Rezūm arm versus -0.9 (95% CI -1.3, -0.5) in the sham arm]. A reduction in BPHII score in Rezūm arm was -3.4 (95% CI -4.0, -2.8) compared to sham arm -1.5 (95% CI -2.3, -0.7). This improvement in QoL persisted for at least 5 years. There was a clinically significant increase of Qmax of 6.2 ± 7.1 mls/s for Rezūm arm, compared with an increase of 0.5 ± 4.2 mls/s for sham (p < 0.0001). There was a non-significant mean decrease of PVR volume -10.6 ± 68.3 mls in the Rezūm arm, compared with increment of 7.2 ± 77.4 mls in the sham arm (p=0.108). Longitudinal data did not report significant improvements up to four years with the exception of three years, which authors claimed to may have been a chance finding.

5.1.5 Rezūm versus medical therapy

Gupta N et al. conducted an evaluation of the long term treatment outcomes over a three years period, comparing the one time application of Rezūm to daily medical treatment.[30] The rate of BPH clinical progression among patients treated either with doxazosin, finasteride or combination therapy was 1.5 to 1.7 per 100 person-year compared with 0.3 per 100 person-year for Rezūm therapy patients. A single procedure Rezūm therapy resulted in a significantly greater mean improvement in IPSS from baseline at 3 months as compared with the 3-month improvement with doxazosin [estimated difference in mean change from baseline (Δ) =2.6; 95% confidence interval (CI) 1.2, 3.9, p<0.001)] or finasteride [Δ=5.2 (95% CI 4.0, 6.4), p<0.001]. The combination drug cohort had similar IPSS improvements at 3 months compared to thermal therapy [Δ=1.4 (95% CI 0, 2.)], p=0.05]. Outcomes were better on average for Rezūm therapy at 6 and 12 months (p=0.02 and p=0.03) followed by similar significant improvements from baseline through 36 months. A significant improvement in the BPHII quality of life measure after Rezūm therapy compared to doxazosin at each visit over 36 months (p=0.02 to p<0.001), and finasteride over 24 months (p=0.03 to p<0.001). The BPHII outcomes were similar between Rezūm therapy and combination drug therapy. Treatment with Rezūm compared with continued use of doxazosin resulted in significantly greater improved peak flow rates over 3 to 12 months (p=0.01 to p=0.03) and greater improvements throughout 36 months compared with finasteride, (p<0.001 to p=0.002). Similarly, Rezūm therapy significantly improved Qmax for up to 12 months compared with combination drug therapy (p<0.001 to p=0.002).[30]

5.1.6 Rezūm versus other MISTs or invasive surgical procedure

An indirect comparison of MIST (Aquablation, Rezūm, and UroLift) to TURP via network meta-analysis was performed by Tanneru K et al.[11] Four RCT were included in the analysis. At all follow up times after 1 month, TURP and Aquablation had higher improvement in IPSS score compared to Rezūm and UroLift ($p<0.05$). The patients in TURP group continued to improve on IPSS at each interval time up to 24 months of follow up while patients in Aquablation and Rezūm had improvements for the first 6 months and had a decline in IPSS improvement score afterwards. At one month of follow up, Aquablation, TURP, and UroLift had comparable and more improvement in QoL compared to Rezūm ($p<0.05$). Aquablation, Rezūm and UroLift had an increase in QoL for the first 6 months whereas TURP group had an increase in QoL up to 12 months followed by a decline at 24 months of follow up. Aquablation and TURP both outperformed Rezūm and UroLift at all interval times in increasing the Qmax ($p<0.05$). Aquablation and TURP had comparable and higher decrease in PVR compared to Rezūm and UroLift ($p<0.05$). (Figure 6)[11]

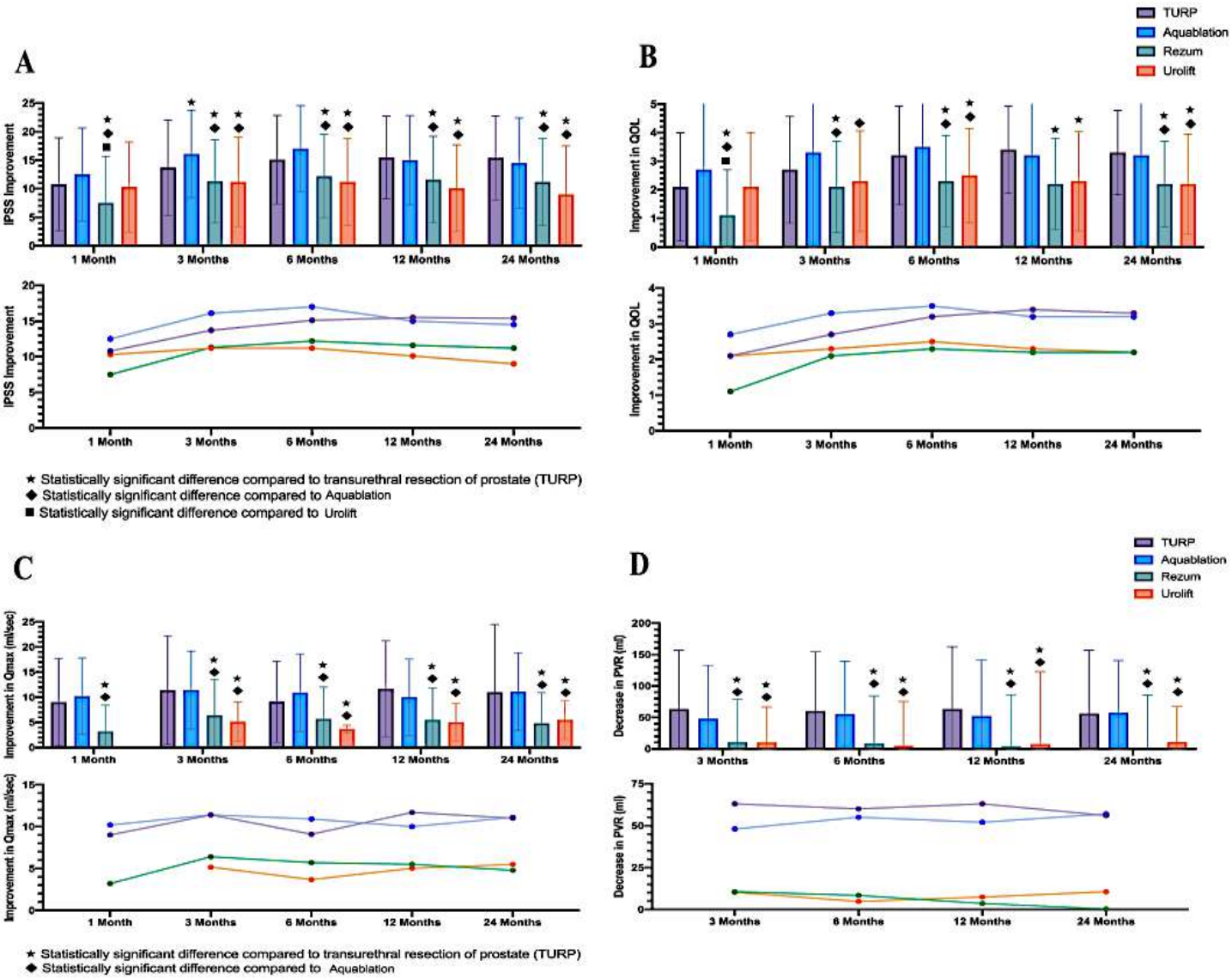

Figure 6: Change from baseline at different follow-up intervals: (A) IPSS; (B) QoL; (C) Qmax; (D)PVR

5.2 SAFETY

The Rezūm system (NxThera, Inc./ Boston Scientific Company, Inc) received European conformity, CE marking in 2013 followed by U.S. Food and Drug Administration (FDA) approval in 2015.[45] An improvement to the existing design was made and the 510(k) FDA approval was given to the modified Nx Thera Rezūm system in March, 2019.[46] The approval indicates the use is for treatment of prostate with hyperplasia of the central zone and/or a median lobe in men aged 50 years or more with a prostate volume between 30mls and 80mls.

5.2.1 Device malfunctions and adverse events

An assessment report produced by the National Institute For Health And Care Excellence (NICE) in 2019 highlighted that a total of 78 records on Rezūm system were found in the FDA Manufacturer and User Facility Device Experience (MAUDE) database. Six records were reports of device malfunctions between May and August,

2019, five of which related to plastic material being out of place and / or obstructing the device, without clinical consequences to the patient. The other 72 records were categorised as injuries, with no deaths reported. Most of reported events were known potential adverse events as listed in the device instructions for use (IFU), with varying degree of severity and duration. The known potential adverse events, include painful urination (dysuria), blood in the urine (haematuria), blood in the semen (haematospermia), decrease in ejaculatory volume, suspected urinary tract infection (UTI) and urinary frequency, retention or urgency.[43]

The reported complications or adverse events of Rezūm procedure were assessed using Clavien–Dindo classification (CDC). The CDC is a standardised system for the registration of surgical complications, categorised based on the severity of a complication/adverse event.[47] The severity is graded according to the type of therapy required to treat the complication (Appendix 3). Grade I and II are classified as minor complications/adverse events, where else Grade III and above are classified as major complications/adverse events.

Six included studies reported on adverse events following Rezūm therapy. There was no occurrence of perioperative device-related or procedure-related adverse events as reported in five studies. Mollengarden et al. did not report on this particular event.[22] Most of the adverse events occurred during first 30 days of therapy. The incidence of adverse events ranged from 41% to 71% between reported studies. Majority of the events were classified as CDC grade I and II. They were transient effects that lasted for two to six weeks.[24, 29, 33, 36] Most common reported adverse events include dysuria (17%-22%)[32-34, 37, 48], UTI (11%-17%)[22, 32], urinary retention (4%-34%)[22, 24, 32-34, 37, 48] and haematuria (11%-18%)[24, 32-34, 37, 48]. Rates of serious adverse events were low across reported studies and these were all related to either sepsis or haematuria requiring return to theater to achieve endoscopic control. Late complication was considered rare. It included bladder neck contracture as reported in two studies[22, 34]. Table 13 demonstrates range of adverse events reported in the included studies.

Garden EB et al. and Bole R et al. reported that there was no differences in rates of minor postoperative complications within one month of Rezūm therapy between large prostates (PV ≥ 80mls) and small prostates.[17, 25] However, Garden EB et al. also reported urgency symptom was more prominent in large prostates compared to small prostates (large prostates (LP): 50.00%, small prostate (SP): 30.36%, p = 0.024). Both groups exhibited similar rates of postoperative UTIs, ED visits, and readmissions within 90 days; however, sub-analysis of urosepsis- related readmissions found statistically significant differences between groups (LP: 5.56%, SP: 0.00%, p = 0.002). Neither group visited the ED (LP: POD 7.75 vs. SP: POD 16.4, p = 0.379) or was readmitted (LP: POD 8 vs. SP: POD 30.5, p = 0.309) sooner, and differences in readmission lengths were similarly insignificant (LP: 2.67 vs. SP: 5.50 days, p = 0.729).[25] Neither group experienced a Clavien grade ≥ III complication.

An indirect comparison of adverse events within 30 days post procedure between Rezūm, UroLift, Aquablation and TURP from four RCTs was made by Tanneru K et al.[11] Rezūm therapy had lower incidence of dysuria (17% versus 34%) and pelvic

pain (2.9% versus 18%) compared to UroLift. Rezūm therapy had higher incidence of dysuria compared to Aquablation and TURP (17% versus 11% versus 6%, respectively). It had lower incidence of urinary retention (4% versus 9%) and UTI (2.9% versus 10%) compared to Aquablation. Patients underwent TURP reported higher incidence of haematuria (33% versus 12%) and urgency (10% versus 5.9%) compared to Rezūm therapy.[11]

Table 13: Adverse events reported in the included studies

Study	Follow-up period	Perioperative device-related or procedure related adverse events	Minor Adverse Event (CDC I-II)		Major Adverse Event (CDC III-IV)	
			Event	% Patients with AEs	Event	% Patients with AEs
Mollengarden[22] *(n =129)*	6 months	Not reported	UTI	17.1	Urinary retention secondary to blood clots requiring return to theater	1.5
			Urinary retention	14.0	Bladder stone requiring cystolithalopaxy	0.8
			Urinary incontinence	3.9	Bladder neck contracture	0.8
			Post void dribllling	3.9		
			Epididymo-orchitis	1.6		
Roehrborn[34] (n=53)	2 years	No	Total: 56 events (12 months)	56.6	Total: 3 events (at 3-12months)	5.6
			Dysuria	18.9	Bladder neck contracture	1.9
			Gross haematuria	11.3	Bladder stone formation	1.9
			Suspected UTI	7.5	Sepsis	1.9
			Urinary retention	5.7		
			Urinary frequency	5.7		
			Heamatospermia	3.8		
			Terminal dribllling	3.8		
Darson[24] *(n=131)*	1 year	No	Urinary retention	10.7		
			Urinary frequency, urgency, haematuria, nocturia	≤3.8		
Dixon[33] (*n=65*)	2 years	No	Total: 115 events ≤ 30 days: 74.8%	69.2	Total: 3 events ≤ 30 days: 100%	1.5
			Dysuria	21.5	3 Grade IIIb events (persistent LUTS - poor stream, frequency, and urinary retention) adjudicated as procedure-related in 1 subject reported at 0-1 months (subsequently underwent TURP at Day 42)	
			Urinary retention	33.8		
			Urinary urgency	20.0		
			Suspected UTI	20.0		
			Haematuria	13.8		
			Poor stream	13.8		
			Urinary frequency	6.2		
			Urinary incontinence	1.5		
			Pain – others	13.9		
			Nocturia	7.7		
			Fever	4.6		
			Urethral secretion (without haematuria or stones)	4.6		
			Terminal dribbling	3.1		

Study	Follow-up period	Perioperative device-related or procedure related adverse events	Minor Adverse Event (CDC I-II)		Major Adverse Event (CDC III-IV)	
			Event	% Patients with AEs	**Event**	% Patients with AEs
Alegorides C[32] *(n=62)*	1 year	No	Total: 63 events ≤ 21 days		No serious adverse events occurred	
			Overactive bladder	22.0		
			Dysuria	20.9		
			Gross haematuria	17.7		
			UTI	11.2		
			Urinary retention	9.6		
			Haemospermia	3.2		
			Blood clots	1.6		
			Pelvic pain	1.6		
			Urinary incontinence	1.6		
McVary[20, 37, 48]	5 years	No	Total: 138 events ≤ 30 days (No late related-AEs occurred from years 1 to 5)	38.2	Total: 3 events ≤ 30 days (No late related-AEs occurred from years 1 to 5)	1.5
			Dysuria	16.9	*De novo* extended urinary retention	0.7
			Gross haematuria	11.8	Nausea and vomiting owing to alprazolam and hospitalized overnight for observation	0.7
			Haematospermia	7.4		
			Urinary frequency	5.9		
			Urinary urgency	5.9		
			Suspected UTI	3.7		
			Urinary retention	3.7		
			Epididymitis	2.9		
			Pain-other	2.9		

5.2.2 Sexual function

Safety evaluations included determination of the rate of *de novo* sexual dysfunction occurring within the first three months after thermal treatment and throughout the follow-up period. Six studies reported on incidence of *de-novo* sexual dysfunction occurring post treatment. Three of these studies reported no new cases.[24, 33] Erectile dysfunction was reported in four men (3.1%) by Mollengarden et al.[22] As no assessment of baseline erectile function was performed in this study, it is unclear whether these cases of erectile dysfunction (ED) were secondary to the treatment. Four studies revealed cases of retrograde ejaculation (RE) with rate of occurrence less than 12%.[22, 23, 29, 32]

Sexual function was evaluated with the International Index of Erectile Function (IIEF) and Male Sexual Health Questionnaire for Ejaculatory Function (MSHQ-EjD) questionnaires.

a. *The International Index of Erectile Function-Erectile Function (IIEF-EF)*

Mean change of erectile function (EF) from baseline is measured as a score on the erection domain of the IIEF questionnaire. Lower scores represent worse sexual function of satisfaction [Erectile Dysfunction (ED) 5-items; 1-7: Severe ED 8-11: Moderate ED 12-16: Mild-moderate ED 17-21: Mild ED 22-25: No ED]. The amount of change in the EF domain needed to be clinically meaningful to patients was evaluated using the criterion of the MCID described by Rosen et al,.[49] For each EF severity category, the MCID would require a minimal EF score difference of 2 for mild erectile dysfunction (ED), difference of 5 for moderate ED, and mean difference of 7 for severe ED.[50]

Six studies included IIEF tool as part of evaluation of treatment impact (Table 14). In most studies, the IIEF parameters remained unchanged at 3 months and no clinically meaningful negative changes in IIEF-EF scores occurred throughout one year follow-up. In study by Dixon et al., the IIEF scores significantly increased at 3-month, 6-month, and 12-month follow-ups (p=0.041 for 12 months). [33] McVary et al. reported that patients who had attempted sexual intercourse did not show a sustained increase in IIEF-EF score over 12 months after treatment. [35, 36, 48]

Table 14: Mean changes in IIEF-EF Score from baseline at different follow-up intervals

STUDY	Mean IIEF-EF Score (± SD) [Change in mean IIEF-EF Score ± SD]						
	Baseline	Follow-Up Interval					
		1 month	3 months	6 months	1 year	2 years	3 years	4 years
Sienna[29] *	20(16-22)	12.5(0.7-21.7) NR	23.5(21-25.5) NR					
Alegorides C[32]	19.4(5.5)	19.6 (5.1) [0.3 (2.5)]	19.8(5.1) [0.5 (2.6)]	20.8(5.2) [0.3 (3.5)]	19.4 (5.6) [0.4 (3.8)]			
Roehrborn[34]	23.2(6.8)	NR NR	21.3(10.3) [-1.9(8.9)]	20.9(9.2) [-0.9(7.4)]	18.8(10.0) [-4.0(8.3)]			
Johnston[23]	15.2	NR NR	17.7 NR	16.8 NR	20.6 NR			
Dixon[33]	13.3(12.0)	10.3(11.6) [-3.0(9.8)]	14.5(11.9) [1.7(10.1)]	15.4(12.0) [1.9(8.9)]	14.1(11.8) [1.5(8.7)]	5.5(11.5) [3.6(6.8)]		
McVary[35, 36, 48]	22.7(7.4)	NR NR	22.7(8.4) [0.1(7.4)]	22.7(8.8) [-0.3(6.4)]	23.0(8.4) [-0.3(7.5)]	21.8(8.7) [-1.2(7.6)]	21.3(9.2) [-1.9(8.2)]	20.8(9.6) [-2.5(8.7)]

*reported in median (IQR); NR = not reported

b*. Male Sexual Health Questionnaire for Ejaculatory Dysfunction (MSHQ-EjD)*

Mean change of ejaculatory function from baseline is measured on the Male Sexual Health Questionnaire for Ejaculatory Dysfunction Short Form (MSHQ-EjD-SF). This was reported as longitudinal function and bother scores. The score of the MSHQ ejaculation function ranged from 0 to 5, with a greater score indicating greater function.[51] The bother domain consisted of one question '*In the last month, if you have had any ejaculation difficulties or have been unable to ejaculate, have you been bothered by this?'*, with assignment of score ranged from 1 to 5. Greater score indicates lesser level of bothersome (1=extremely bothered, 2=very bothered, 3=moderately bothered, 4=a little bit bothered and 5=not at all bothered). A change in MSHQ scores less than 0 point representing worsening in sexual function and more than 0 representing improvement in sexual function.[52]

Four studies included MSHQ-EjD-SF tool as part of evaluation of treatment impact (Table 15). As demonstrated by included studies, the ejaculatory function remained stable up to one year. Studies by McVary et al. [35, 36, 48] and Dixon et al. [33] showed a longer preservation of function up to two years. McVary et al. reported in their study that there were significant declines to 8.4 ± 4.5 (n = 64, p = 0.046) and 8.2 ± 4.6 (n = 56, p = 0.038) at three and four years respectively. Contrarily, all studies displayed declining bother score from baseline as early as one to three months post procedure. However, the level of bothersome remained stable beyond three months period.

Table 15: Mean changes in MSHQ-EjD Score from baseline at different follow-up intervals

STUDY		Mean MSHQ-EjD (± SD) [Change in mean MSHQ-EjD (± SD)]							
		Baseline	Follow-Up Interval						
			1 month	3 months	6 months	1 year	2 years	3 years	4 years
Alegorides C[32]	Function	8.6(5)	5.7 (6.9)	9.5(5)	11.9 (2.9)	10(3.5)			
			[−1.8(4.5)]	[1.25(3)]	[2.9(3.7)]	[2.1(4)]			
	Bother	2.0 (1.7)	1.75(1.8)	1.2(1.1)	0.7(0.9)	0.9 (1.1)			
			[−0.25(1)]	[−0.7(1.1)]	[−1.3(1.3)]	[−1.3(1.7)]			
Roehrborn[34]	Function	9.9(3.8)	NR	9.7(5.1)	8.6(4.9)	9.1(4.6)			
			NR	[-0.2(4.0)]	[-1.2(3.8)]	[-0.7(3.7)]			
	Bother	1.6(1.7)	NR	1.6(1.6)	1.8(1.7)	2.1(1.9)			
			NR	[-0.1(2.0)]	[0.0(1.8)]	[0.4(1.7)]			
Dixon[33]	Function	5.9(4.8)	5.6(6.1)	7.1(5.0)	8.0(4.5)	5.0(4.7)	7.0(4.8)		
			[-0.2(3.9)]	[1.2(4.6)]	[2.5(4.9)]	[-0.3(5.8)]	[2.4(5.2)]		
	Bother	2.3(2.3)	0.8(0.9)	0.9(1.1)	1.0(0.9)	0.9(0.8)	0.8(0.5)		
			[-1.5(2.7)]	[-1.4(2.4)]	[-1.5(2.5)]	[-1.3(2.3)]	[-1.9(2.0)]		
McVary[35, 36, 48]	Function	9.3(3.1)	NR	9.7(4.5)	9.7(4.0)	9.3(4.0)	9.1(4.4)	8.5(4.5)	8.2(4.6)
			NR	[0.3(4.3)]	[0.1(3.6)]	[-0.3(3.5)]	[-0.5(4.2)]	[-1.4(3.8)]	[-1.8(4.4)]
	Bother	2.2(1.7)	NR	1.8(1.7)	1.8(1.5)	1.5(1.5)	1.7(1.7)	1.6(1.5)	2.0(1.7)
			NR	[-0.3(1.9)]	[-0.4(1.9)	[-0.7(1.8)]	[-0.5(1.7)]	[-0.5(1.6)]	[-0.1(1.8)]

Impact on sexual function following Rezūm therapy versus medical treatment

McVary et al.[50] compared sexual function over three years after a single Rezūm therapy versus continuous daily treatment with pharmaceutical agents in the Medical Therapy of Prostatic Symptoms (MTOPS) study in subjects with matched criteria for LUTS severity and prostate size. Sexual function data from sexually active cohorts in the MTOPS study (1,209 subjects) randomized to doxazosin, finasteride, combination drugs and placebo, and sexually active men who received Rezūm therapy (86 subjects). Men receiving combination drug therapy had the greatest percentage of change in EF at one year of -10.5%, compared with -6.4% for doxazosin and -5.3% for finasteride; these estimated percentage change in mean scores continued at a similar level, or with further score decreases over three years (all p ≤ 0.004). The profiles of EF scores for Rezūm was without significant mean changes over 3 years relative to baseline scores. The study also revealed that

combination therapy resulted in the greatest estimated mean percentage change in ejaculatory function relative to baseline of -18.9% at year 1 to -16% (-20.6, -11.4) at year 3 (p <0.001). The score decreased at 8.2% after finasteride and further decreased at year 3 with mean percentage change of -11.3% (-15.3, -7.3), p< 0.001. Subjects treated with thermal therapy showed a profile of decreasing, but no significant mean change in ejaculatory function at year 3, percentage change of -9.2% (95% CI -18.4,-0.0), p= 0.05.

Impact on sexual function following Rezūm therapy versus UroLift, Aquablation and TURP

Based on indirect comparison by Tanneru K et al.[11], patients undergoing UroLift had no reported incidence of ED or RE. Rezum therapy resulted in 2.9% RE however no occurrence of ED reported. Patients undergoing TURP reported higher incidence of ED (19%) and RE (22%). Aquablation was reported to have resulted in 6% RE. The data of MSHQ-EjD (function) changes was available for follow up intervals after 3 months. Patients in UroLift had an improvement in their MSHQ-EJD scores at all follow up time, this improvement was significant compared to TURP group at all follow up times (p<0.05), and compared to Aquablation, and Rezūm at 6 and 12 months, respectively (p<0.05). The MSHQ score decreased over time for all interventions, except Aquablation which demonstrated an increasing pattern during the follow up intervals (Figure 7). There was no specific trend in change of MSHQ-EjD bother score. Initially, the patients in UroLift had a reduction in bother score which was significant compared to Aquablation and TURP at 3 months (p<0.05). This difference was not significant at 6 or 24 months. At 12 months, UroLift patients had significant reductions in bother score compared to Rezūm, Aquablation and TURP.

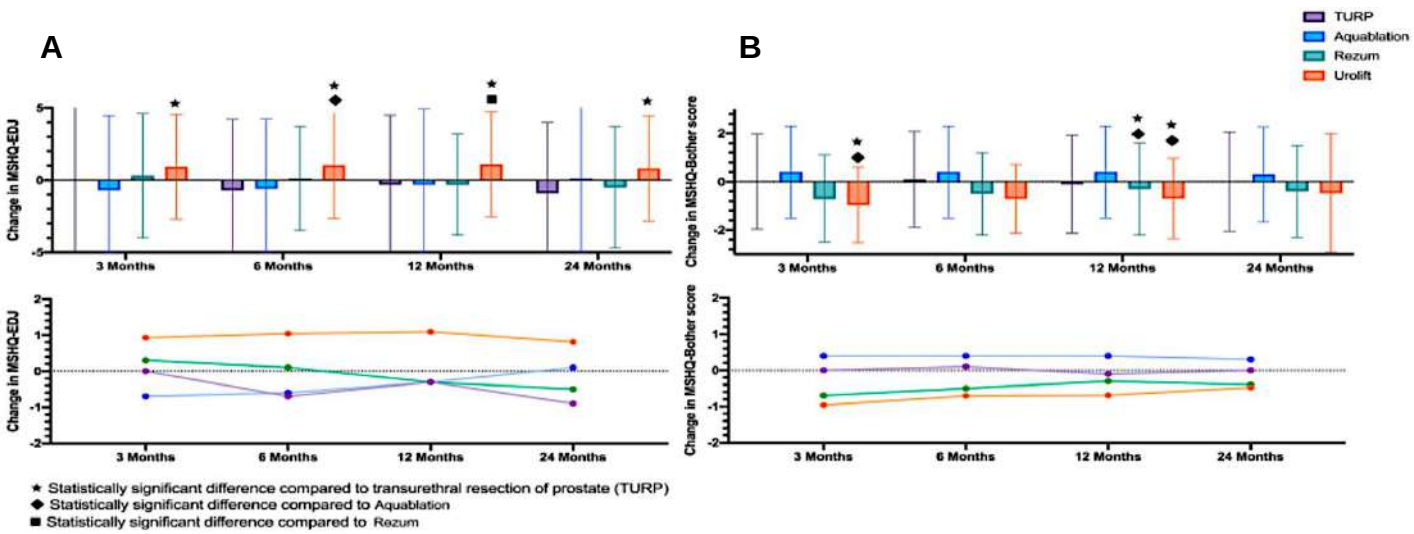

Figure 7: Change from baseline at different follow-up intervals: (A) MSHQ-Ejd (Function); (B) MSHQ-Ejd (Bother)

5.2.3 Retreatment rate

Surgical retreatment

The durability of the procedure is reflected by retreatment rate. Surgical retreatment rate for Rezūm therapy was reported to be 2% at six months (two studies)[22, 29], 1-3% at one year (three studies)[23, 24, 37], 4% at two years (one study)[37], 4.4% at three years (one study)[37] and 4.4% at five years follow up (one study)[37]. A higher retreatment rate (8.33%) at was seen with large prostates cohort at one year follow-up.[25] However, The difference in mean time to retreatment was statistically insignificant between groups (LP 367 days, SP 364 days, p = 0.909).[25] The surgical procedures included repeat Rezūm therapy[22], TURP[33], open prostatectomy (2), and photovaporization[22]. Rezūm therapy had lower surgical retreatment rate in comparison to UroLift (4% versus 7.5%) at two years follow-up, however reported a higher retreatment rate compared to TURP (4% versus 1.5%).[11]

Medical retreatment

Initiation of BPH oral medication after a minimally invasive procedure also serves as an indication of durability. Following Rezūm therapy at one, two, three, four and five years, the incidence of patients that initiated the use of pharmacotherapy with alpha blockers was 0.7%, 2.2%, 3.7%, 5.2% and 11.1% respectively (one study).[37]

5.3 COST/COST-EFFECTIVENESS

There was no published data available on the price of Rezūm device and procedure in Malaysia during the time of this review.

In United State, the list price of the Rezūm delivery device (single use) is US$1,400 per device with the average selling prize is around US$1,150.[53] The cost of Rezūm procedure derived from 2016 Medicare national average fee schedules, is reported to be US$2,489 (inclusive of the cost for pre-operative assessment with cystoscopy, transrectal ultrasound (TRUS), urodynamic study (UDS), post-operative assessment and one year follow up appointment). The cost is cheaper in comparison to TURP

(US$4,821) and Urolift (US$6,230).[54] The national average Medicare reimbursement for Rezūm procedure is approximately US$1,950 when performed in the office.[53]

A cost analysis of Rezūm procedure and TURP was conducted by Haroon UM et al., using real-time cost to the institution per case. When Rezūm procedure compared to ten matched patients undergoing TURP during the same period in an Irish hospital, there was a significant cost saving of €1986.52 per patient for Rezūm, overall up-front cost saving of €22,819 with an additional 19 bed days and 5 theatre hours spared.[31] Both procedures were done under general anaesthesia, as inpatient cases. If Rezūm procedure was performed as purely daycare case and patients be discharged from daycare ward on the same day, further saving of €623 saving per Rezūm patient compared to TURP could be achieved.[31]

An economic model reported by NICE, estimated that over a 4-year period, Rezūm was able to provide savings of £497, £569 and £651 compared to UroLift, TURP and Holmium Laser Enucleation of the Prostate (HoLEP) respectively.[43] The analysis was conducted from the National Health Service (NHS) perspective. Rezūm remained cost-saving when all parameters were subjected to one-way deterministic sensitivity analysis (DSA). Scenario analysis, which investigated the effect of erectile dysfunction in a subgroup of sexually active men, did not materially affect the direction or magnitude of results. The PSA indicated there was a ≥ 97.5% chance Rezūm was cost-saving compared with UroLift, TURP and HoLEP.[43]

A study by Ulchaker JC et al. reported a cost-effectiveness analysis (CEA) framework using a cohort Markov decision analytic model.[54] This study adopted a 2-year time horizon from an American third party payer perspective with both costs and effects discounted at 3% annually. It compared six treatment options in men with symptomatic BPH. The six treatments included were

i. Combination prescription drugs therapy (ComboRx), an inhibitor of 5α-reductase (e.g., dutasteride or finasteride), and an α-selective adrenergic receptor blocker (e.g., tamsulosin or doxazosin)

Minimally invasive treatments

ii. The Rezūm® System (radiofrequency thermal therapy procedure)
iii. The Prostiva® RF Therapy System (radiofrequency thermal therapy procedure)
iv. The UroLift® System (prostatic urethral lift, permanent implants to retract enlarged prostate tissue)

Invasive surgical procedures

v. Greenlight® laser photovaporization of the prostate (PVP)
vi. TURP

Rezūm therapy dominated treatment with UroLift, and being slightly more efficacious, as shown in Table 16. Probabilistic sensitivity analysis (PSA) indicated that there was a 100% chance that Rezūm was both less costly and more effective than UroLift. A comparison of Rezūm and Prostiva, showed Rezūm to be slightly more expensive about 66% of the time and more effective about 97% of the time,

indicating that the costs are unlikely to differ much, but offering strong evidence of a point difference in effectiveness. The more invasive procedures (TURP and Greenlight PVP) were both more effective than Rezūm, but also considerably more costly.[54] As shown in Figure 8, the most efficient treatments, those that result in the greater symptom relief for the money spent, are found along the production possibility frontier, the line connecting the southeastern most treatments.

Table 16: Costs, effectiveness and ICERs of the treatments over a 2-year horizon

Treatment	**Mean Cost at 2 years***(US$)	**Mean IPSS at 2 years****	**ICER** (US$)
Pharmacotherapy			
Medicare Part D price	1,736	18.9	97
Branded	7,082	18.9	-518
Rezūm	2,582	10.2	Base comparator
UroLift	6,386	11.4	-3,058 **DOMINATED**
Prostiva	2,855	10.9	-352
Greenlight PVP	5,099	7.4	900
TURP	5,181	6.4	686

*Mean costs at 2 years (including diagnostic work up, initiation cost (for pharmacotherapy), post-procedure assessment, and 1 year check-up management of adverse events).
**A common baseline IPSS of 22 was used for comparison of the treatment modalities in the model. 3-point improvement in symptom score is set as the minimum meaningful clinical improvement score.

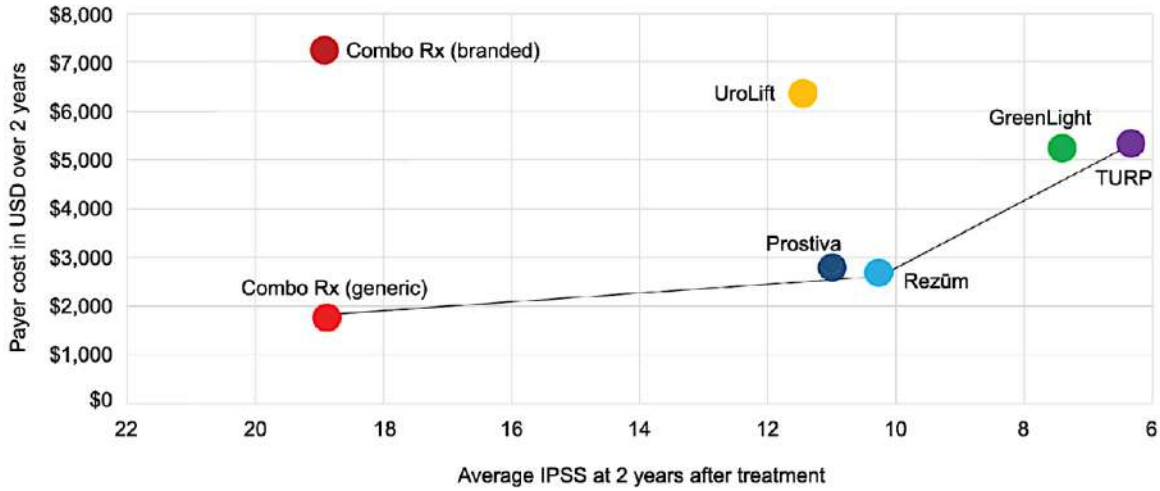

Figure 8: Production possibility frontier graph for average costs of the six therapies relative to cost-effectiveness over 2 years

Chughtai B et al. used long-term efficacy and safety data from the UroLift and Rezūm RCTs to evaluate the cost-effectiveness and budget impact of both treatments from US Medicare perspective for men with BPH experiencing moderate-to-severe LUTS.[55]

The cost-effectiveness was evaluated over a 4-year time horizon, using a willingness-to-pay threshold of US$50,000 per quality-adjusted life-year (QALY) gained. Similarly with previous study, the CEA showed that Rezūm was more effective and less costly treatment strategy than UroLift. At four years, Rezūm was associated with lower retreatment rates (10.9% versus 24.6%), higher QALYs (3.548 versus 3.490) and lower total costs (US$2233 versus US$7393) compared with

UroLift. The Budget Impact Model demonstrated that 70% total cost difference of UroLift and Rezūm was predominantly driven by higher UroLift procedural (US$5617 versus US$1689) and retreatment (US$976 versus US$257) costs (Figure 9). The PSA demonstrated that relative to UroLift, Rezūm yielded higher QALYs and lower costs 99% and 100% of the time, respectively.

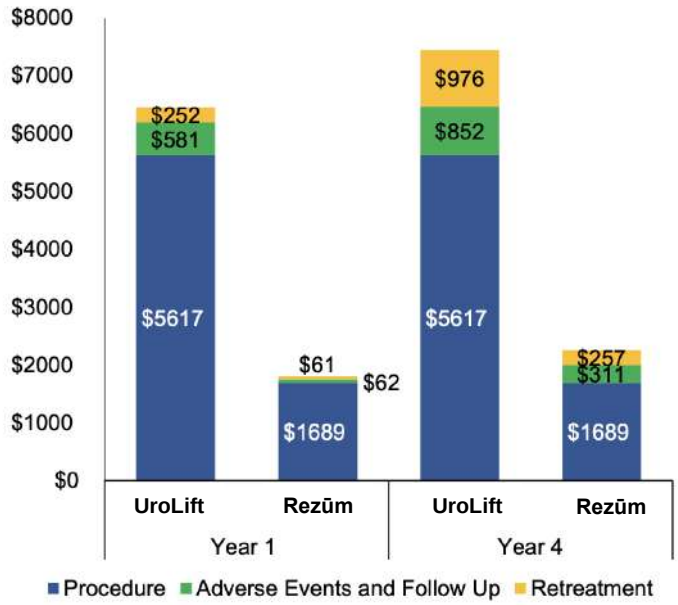

Figure 9: Medicare Per Patient Costs of UroLift and Rezūm at Year 1 and Year 4

5.4 ORGANISATIONAL

5.4.1 International Guidelines

The American Urological Association (AUA) and NICE guidelines have accepted Rezūm therapy as one of the MIST options for the management of LUTS secondary to BPH.[45, 56, 57] While the European Association of Urology (EAU) guideline has listed Rezūm therapy among the techniques under investigation.[58] In United Kingdom, Rezūm procedure was integrated into the treatment options for LUTS in males with an enlarged median prostatic lobe, by NICE in 2018. It is considered as an alternative treatment to TURP or HoLEP for men with moderate to severe LUTS with prostate volume between 30mls to 80mls.[45] Similarly, in United States, the AUA 2021 guideline recommends the use of Rezūm therapy for prostates with volume less than 80mls. The guideline states that Rezūm therapy may be offered as a treatment option to eligible patients who desire preservation of erectile and ejaculatory function (conditional recommendation; Grade C evidence).[45, 46] However, the EAU 2020 guideline does not provide a clear statement regarding Rezūm therapy adoption as treatment option for BPH. It considers the need for RCTs against a reference technique to confirm the efficacy, safety and durability of the procedure.[58]

5.4.2 Treatment delivery

Procedural time

Four studies reported on the procedural time alongside the number of injections given per subject and baseline prostate volume. The procedural time ranged between four to 11 minutes. As shown in the Table 17, the time taken to perform the procedure is directly associated with baseline volume of the prostate and number of vapour injection given. Rezūm therapy had been shown to have a shorter procedural time compared to UroLift (range: 55±17 to 66±24 minutes), Aquablation (33±16 minutes) and TURP (35±15 minutes).[11]

Table 17: Mean procedural time and number of steam injections per subject in the included studies

STUDY	Mean baseline prostate volume ±SD (mls)	Mean Procedural Time (Initial insertion of device until complete removal) ±SD (in minutes)	Mean number of injections/subject ±SD
Roehrborn[34]	44.5 ± 13.3	4.4 ± 1.7	5.1 ± 1.9
Mcvary[35-37]	45.9 ± 12.9	5.3 ± 3.5	4.5 ± 1.8
Alegorides C[32]	54.3 ± 28.4	*6 (3—19)	* 5 (2—11)
Sienna [29]	*60 (45–78)	*10.5 (8.7–15.0)	*7 (IQR 5–8)

* reported as median (IQR)

Sedation and pain management

Five studies included information on the type of sedation and pain management given to their patients.[22, 24, 29, 30, 32] McVary et al. reported that 69% of their patients underwent Rezūm procedure using oral sedation, 10% of the patients required intravenous (IV) sedation and 21% of the patients were given prostatic block for the procedure.[35] Another study conducted by Dixon et al. also had majority of their Rezūm treatment done using oral sedation (79%) and the remaining were done using IV sedation (21%).[33] Darson et al. had their procedures performed with IV sedation (86%), general anaesthesia (15%) or under prostatic block (6%).[24] While in study by Mollengarden D et al., the procedure was done under prostatic block with the use of urethral local anaesthetic injection for all the included patients.[22] Alegorides C et al. had 81% of their patients under general anaesthesia and 19.3% under hypnosis (two patients had hypnosis alone, seven patients had slight sedation and/or supplementary antalgic and three patients changed over to general anaesthesia for comfort reasons**)**.[29] All the Rezūm procedures in these studies were reported to have been completed successfully without any serious procedure-related complication.

Length of hospital stay (LOS)

Tanneru K et al. described in their systematic review, the length of hospital stay associated with different MIST options as well as TURP as gold standard treatment.[11] The majority of patients undergoing Rezūm and UroLift were discharged on the same day. The mean length of stay (LOS) for patient's admitted

after undergoing UroLift was 1±1 day and those undergoing TURP or Aquablation had a median LOS of 1.4 days.

Post-operative catheterisation

Placement of post-operative urinary catheter is normally because of urologist standard protocol. Duration of catheterization is at the discretion of treating urologist which varies by different practices. Based on the finding from six studies[21, 22, 29, 32, 33, 37], the mean duration of post-operative catheterization ranged between 3.4±3.2 days and 4.5 ± 3.8 days.

Recovery

It was reported by Tanneru K et al. that patients undergoing Rezūm therapy returned to preoperative activity level at median of 4 days after catheter removal.[11] The mean length of time taken for return of pre-operative activity level ranged between 8.6±7.5 days and 11±19 days after undergoing UroLift. In comparison, men undergoing, TURP went to preoperative activity level on an average of 17±19 days.[11]

5.4.3 Training

Expert opinion claimed it should be a straight forward procedure for urologists with sufficient endoscopic experience.[59] The available training includes 1-day masterclass with lectures, demonstration of how the procedure being done and practicing on a simulator. According to NICE report, the company representative provided support for the first ten cases and also trained the staff on how to set up the equipment.[43] Alegorides C et al. reported the learning curve for Rezūm procedure in their study was three cases.[32]

5.5 SOCIAL

Procedural Satisfaction

Three studies [21-23] explored the level of patient satisfaction with Rezūm therapy. Mollengarden D et al. revealed that the mean score based on 5-point scale rating for experience satisfaction and treatment outcome satisfaction were 4.2 and 4.0 respectively. A total of 77% of patients were satisfied with the experience and 65% of the patients were satisfied with the outcome of the procedure. Majority of the patients (86%) said they would recommend the procedure to a friend in similar circumstances.[22]

Johnston et al. reported 89% of the patients in their study were satisfied with the procedure.[23] In a study by Tutrone RF et al., when comparison was made between UroLift and Rezum therapy, UroLift patients seemed to be more satisfied with the experience and the outcome of the treatment (p=0.08). No published study available that compared level of satisfaction between Rezum therapy with the rest of MISTs or TURP.

6.0 LIMITATION

This technology review has several limitations. Only English full text articles were included in this review. Hence, there is a possibility that potentially relevant studies published in languages other than English could have been missed. The findings and interpretations are limited by the quality and quantity of available evidence. To date, there is only one RCT published on this technology. All the included studies also have a small sample size which limit the generalisability of the findings.

7.0 CONCLUSION

Rezūm therapy demonstrated the ability to improve urologic symptoms and quality of life, and to slow down the rate of clinical progression among BPH patients. Its effectiveness was comparable to UroLift, but inferior to Aquablation and the gold standard TURP procedure. Application of Rezūm therapy for large sized prostates (80-120mls) showed comparable improvement with small sized prostates (<80mls). Majority of BPH patients who underwent Rezūm therapy experienced transient minor adverse effects, which include dysuria, UTI, urinary retention and haematuria. No *de novo* erectile dysfunction was observed. Lower rate of retrograde ejaculation was reported. Rezūm therapy was shown to be a cost-saving procedure in comparison to other MISTs and invasive BPH surgeries (HoLEP and TURP). The net cost saving was significantly associated with its lower procedural cost, (inclusive of preoperative assessment and follow-up visits), reduction in bed days and operation theatre hours spared. There was a high level of satisfaction with Rezūm procedure among the patients, either with the experience or with the outcome of the procedure.

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Appendix 1: HIERARCHY OF EVIDENCE FOR EFFECTIVENESS STUDIES

DESIGNATION OF LEVEL OF EVIDENCE

I Evidence obtained from at least one properly designed randomised controlled trial.

II-I Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III Opinions or respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

SOURCE: US/CANADIAN PREVENTIVE SERVICES TASK FORCE (Harris 2001)

Appendix 2: SEARCH STRATEGY

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily (1946 to September 28, 2021)

Search strategy

#	Search Details	Results
1	PROSTATIC HYPERPLASIA/	22680
2	benign prostatic hyperplasia.tw	14386
3	benign prostatic hypertrophy.tw	2049
4	(prostatic adj1 (hyperplasia or hypertrophy)).tw	17470
5	(benign prostatic adj1 (hyperplasia or hypertrophy)).tw	16298
6	rezum.tw	104
7	LOWER URINARY TRACT SYMPTOMS/or DYSURIA/ or NOCTURIA/ or PROSTATISM/ or URINARY BLADDER, OVERACTIVE/ or URINARY BLADDER, UNDERACTIVE/ or URINARY INCONTINENCE/	32299
8	lower urinary tract symptom*.tw	9037
9	dysuria.tw	4590
10	nocturia.tw	3610
11	prostatism.tw	601
12	(urinary bladder adj (overactive or underactive)).tw	3
13	urinary incontinence.tw	25287
14	"Quality of Life"/	222570
15	"Quality of Life".tw	313638
16	IPSS.tw	4920
17	Qmax.tw	2476
18	"post void volume".tw	7
19	URINARY BLADDER NECK OBSTRUCTION/	4538
20	urinary bladder neck obstruction.tw	3
21	URINARY RETENTION/	4816
22	(urinary adj retention).tw	9593
23	"COSTS AND COST ANALYSIS"/	50022
24	(cost adj1 analys#s).tw	8298
25	(cost analys#s adj2 cost$1).tw	7881
26	(cost minimi#ation adj1 analys#s).tw	802
27	(cost adj1 comparison$1).tw	1336
28	(cost adj1 measure$1).tw	765
29	COST BENEFIT ANALYSIS/	86630
30	(cost benefit adj1 data).tw	21
31	(cost adj1 effectiveness).tw	64818
32	(economic adj1 evaluation$1).tw	13038
33	1 or 2 or 3 or 4 or 5	28133
34	7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22	421393
35	23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32	172316
36	6 and 33 and 34	115
37	6 and 35	6
38	36 or 37	118

Database : PUBMED

Search strategy

#	Search Details	Results
1	((((benign prostatic hyperplasia)) OR (benign prostatic hyperplasia[MeSH Terms])) OR (benign prostatic hyperplasia[Text Word])) AND (rezum)	102
2	((((((((((((((((((((((((((lower urinary tract symptom) OR (lower urinary tract symptom[MeSH Terms])) OR (lower urinary tract symptom[Text Word])) OR (dysuria)) OR (dysuria[MeSH Terms])) OR (dysuria[Text Word])) OR (nocturia)) OR (nocturia[MeSH Terms])) OR (nocturia[Text Word])) OR (prostatism)) OR (prostatism[MeSH Terms])) OR (prostatism[Text Word])) OR (urinary bladder overactive)) OR (urinary bladder overactive[MeSH Terms])) OR (urinary bladder overactive[Text Word])) OR (urinary bladder underactive)) OR (urinary bladder underactive[MeSH Terms])) OR (urinary bladder underactive[Text Word])) OR (urinary incontinence)) OR (urinary incontinence[MeSH Terms])) OR (urinary incontinence[Text Word])) OR (Quality of Life)) OR (Quality of Life[MeSH Terms])) OR (Quality of Life[Text Word])) OR (urinary bladder neck obstruction)) OR (urinary bladder neck obstruction[MeSH Terms])) OR (urinary bladder neck obstruction[Text Word])) OR (urinary retention)) OR (urinary retention[MeSH Terms])	749,842
3	((((((((((((costs and cost analysis) OR (cost analysis[MeSH Terms])) OR (analyses, cost[Text Word])) OR (cost analysis[Text Word])) OR (cost benefit analysis[Text Word])) OR (cost effectiveness)) OR (cost effectiveness[MeSH Terms])) OR (cost effectiveness[Text Word])) OR (economic evaluation)) OR (economic evaluation[MeSH Terms])) OR (economic evaluation[Text Word])) OR (cost comparison)) OR (cost comparison[MeSH Terms])) OR (cost comparison[Text Word])	347,598
4	#1 AND #2	102
5	#1 AND #3	7
6	#4 OR #5	102

Appendix 3

Clavien-Dindo Classification of Surgical Complications

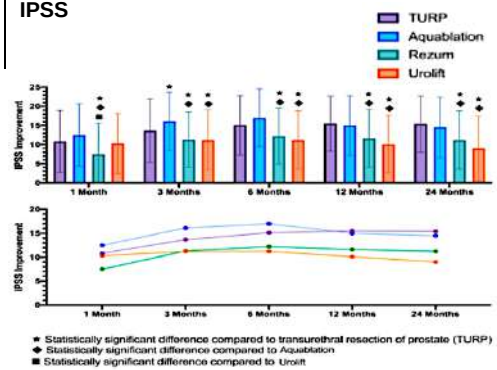
Grade	Definition
I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside.
II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included
III	Requiring surgical, endoscopic or radiological intervention
IIIa	Intervention not under general anaesthesia
IIIb	Intervention under general anaesthesia
IV	Life-threatening complication (including CNS complications)* requiring IC/ICU management
IVa	Single organ dysfunction (including dialysis)
IVb	Multiorgan dysfunction
V	Death of a patient

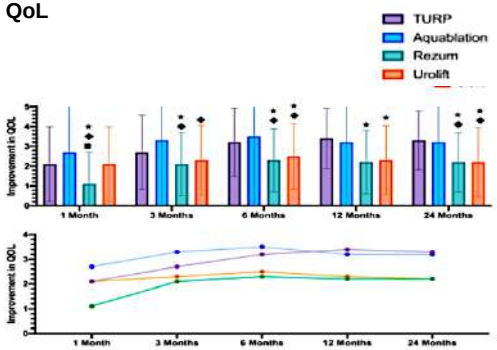
*Brain hemorrhage, ischemic stroke, subarachnoid bleeding, but excluding transient ischemic attacks.

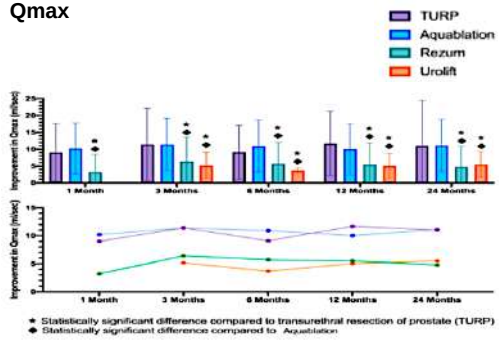
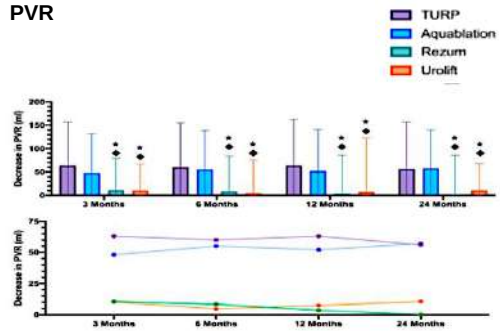
CNS, central nervous system; IC, intermediate care; ICU, intensive care unit.

Appendix 4

Evidence Table : Effectiveness and safety
Question : How effective and safe is the Rezūm therapy for management of LUTS secondary to BPH?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
1. Tanneru K, Jazayeri SB, Alam MU et al. An Indirect Comparison of Newer Minimally Invasive Treatments for Benign Prostatic Hyperplasia: A Network Meta-Analysis Model. J Endourol. 2021;35(4):409-416.	Network meta-analysis **Objective:** To provide an indirect comparison of the urinary and sexual domain outcomes and complications following newer minimally invasive surgical therapy (MIST) of Aquablation, Rezum, and UroLift for benign prostatic hyperplasia (BPH) to transurethral resection of prostate (TURP). **Methods:** - Databases: Embase, Medline through PubMed, and Cochrane databases. Databases were screened for RCTs reporting outcomes after Aquablation, Rezum and UroLift. - Exclusion criteria: patients with prostates more than 80mls - Risk of bias assessment using ROB 2.0 - Outcomes: IPSS, QoL, Qmax, PVR, MSHQ-EjD Function and Bother	**I**	4 studies included (UroLift -2 studies, Rezum - 1 study and Aquablation – 1 study) TURP was used as the control group in two studies and sham procedure in the other two studies. Baseline characteristics of participants of included studies: **Rezūm (Mc Vary et al, 2016)** N=136 Age Mean ± SD: 63 ± 7.1 Prostate volume (ml): 54.8 ± 13 IPSS: 21.4 ± 4.5 QoL: 4.3 ± 1.0 Qmax: 9.8 ± 2.3 PVR: 84.9 ± 54.0 MSHQ-EjD Function: 9.6 ± 3.0 MSHQ-EjD Bother: 2.2 ± 1.7 **UroLift (Roehrborn et al,2013)** N=181 Age Mean ± SD: 67 ± 8.6 Prostate volume (ml): 44.5 ± 12.4 IPSS: 21.8 ± 5.6 QoL: 4.5 ± 1.0 Qmax: 8.3 ± 2.4 PVR: NA MSHQ-EjD Function:8.7± 3.3 MSHQ-EjD Bother: 2.2 ± 1.7	Rezūm therapy	UroLift, Aquablation, TURP	24 months	**IPSS**  **-** At all follow up times after 1 month, TURP and Aquablation had higher improvement in IPSS score compared to Rezum and UroLift ($p<0.05$) -TURP and Aquablation had similar IPSS improvement scores except at 3 months where Aquablation had higher improvements compared to TURP. -The patients in TURP group continued to improve on IPSS at each interval time up to 24 months of follow up while patients in Aquablation and Rezum had improvements for the first 6 months and had a decline in IPSS improvement score afterwards. - Patients in the UroLift group had an initial improvement for the first 3 months and had a steady decline in improvement afterwards. Supplementary Table 2 shows the detail -At 24 months, patients undergoing Aquablation had an average of 3.3, 95% CI 0.4 - 6.2, and 5.4, 95% CI 2.7 - 8.1 higher improvement compared to patients undergoing Rezum and UroLift, respectively.

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
			UroLift (Sonksen et al, 2015) N=116 Age Mean ± SD: 63 ± 6.8 Prostate volume (ml): 38 ± 12 IPSS: 21.4 ± 5.5 QoL: 4.6 ± 1.1 Qmax: 9.3 ± 3.4 PVR: 80.5 ± 61.0 MSHQ-EjD Function:11 ± 2.7 MSHQ-EjD Bother: 1.7 ± 1.8 **Aquablation (Gilling et al, 2018)** N=116 Age Mean ± SD: 66 ± 7.3 Prostate volume (ml): 54.1± 16.2 IPSS: 22.9 ± 6 QoL: 4.8 ± 1.1 Qmax: 9.4 ± 3 PVR: 97 ± 79 MSHQ-EjD Function:8.1± 3.7 MSHQ-EjD Bother: 2 ± 1.6				**QoL**  -At all follow up times Aquablation and TURP had comparable improvements in QoL. -At 1 month of follow up, Aquablation, TURP, and UroLift had comparable and more improvement in QoL compared to Rezum ($p<0.05$). -After 3 months, Rezum and UroLift, had lower improvements in QoL compared to both Aquablation and TURP at all follow up intervals ($p<0.05$). -There was no difference between Rezum and UroLift at 24 months of follow up. -Aquablation, Rezum, UroLift had an increase in QoL for the first 6 months whereas TURP group had an increase in QoL up to 12 months followed by a decline at 24 months of follow up. -At 24 months of follow up, patients in Aquablation had an average of 1.0, 95% CI: 0.2 - 1.9 and 1.0, 95% CI: 0.2 - 1.8 higher improvement in QoL compared to Rezum and UroLift patients, respectively ($p<0.05$).

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
							Qmax  - At all follow up times, Aquablation and TURP had higher and comparable improvement in Qmax scores. - Aquablation and TURP both outperformed Rezum and UroLift at all interval times in increasing the Qmax ($p<0.05$). -There was no difference between Rezum and UroLift in any interval time. -Patients in Aquablation group had an average of 6.3, 95% CI 1.8 - 10.9, and 6.9 95% CI, 3.0 - 10.9 higher improvement in Qmax in comparison to Rezum and UroLift, respectively ($p<0.05$). **PVR** 

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
							-Aquablation and TURP had comparable and higher decrease in PVR compared to Rezum and UroLift ($p<0.05$). -The decrease in PVR remained relatively stable at 24 months of follow up in Aquablation, TURP, and UroLift, while there was a declining pattern in patients undergoing Rezum. -There was no difference between Rezum and UroLift at any follow up time - At 24 months of follow up, Aquablation patients had higher decrease in PVR compared to Rezum and UroLift with an average of 56.7 95% CI 19.4 – 94.0, and 46.4 95% CI 7.9 – 84.9 ml lower PVR, respectively ($p<0.05$). **Sexual function** *MSHQ-EJD (Function)* -Patients in UroLift had an improvement in their MSHQ-EJD scores at all follow up time, this improvement was significant compared to TURP group at all follow up times ($p<0.05$), and compared to Aquablation, and Rezum at 6 and 12 months, respectively ($p<0.05$). -The MSHQ score decreased over time for all interventions, except Aquablation which demonstrated an increasing pattern during the follow up intervals. *MSHQ-EJD (Bother)* -There was no specific trend in change of bother score. -Initially, the patients in UroLift had a reduction in bother score which was significant compared to Aquablation and TURP at 3 months ($p<0.05$). This difference was not significant at 6 or 24 months. At 12 months, UroLift patients had significant reductions in bother score compared to Aquablation and TURP. **Adverse events** -There was a higher incidence of dysuria and pelvic pain following UroLift. -Patients undergoing UroLift had no reported incidence of erectile dysfunction (ED) or retrograde ejaculation (RE).

<table>
<tr><th>Bibliographic citation</th><th>Study Design/ Methods</th><th>LE</th><th>Number of Patients & Patient Characteristics</th><th>Intervention</th><th>Comparison</th><th>Length of Follow-up (If Applicable)</th><th>Outcome Measures/Effect Size</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>-Patients undergoing TURP reported higher incidence of bleeding, urgency, urge incontinence, ED, and RE.
-After Aquablation, there was a higher incidence of urinary retention and urinary tract infection.
-At two years of follow up, the retreatment rates following Aquablation, Rezum, TURP and UroLift were 4.3%, 4%, 1.5%, and 7.5%, respectively.</td></tr>
</table>

	UroLift (n=181)	Rezum (n=134)	Aquablation (n=116)	TURP (n=100)
Dysuria	48 (34%)	23(17%)	12(11%)	6 (6%)
Hematuria	54 (29%)	16(12%)	18 (15%)	33 (33%)
Urgency	10 (7%)	8 (5.9%)	5 (4%)	10 (10%)
Urge incontinence	6 (3%)	NR		
Erectile Dysfunction	0	0	NR	19 (19%)
Retrograde Ejaculation	0	4 (2.9 %)	7 (6%)	22 (22%)
Urinary retention	5 (3%)	5(4%)	10 (9%)	4 (4%)
UTI	7 (4%)	4 (2.9%)	11(10%)	6 (6%)
Pelvic pain	25 (18%)	4 (2.9%)	9 (8%)	5 (5%)

NR- Not Reported, UTI- Urinary tract infection, TURP- Transurethral resection of prostate

Evidence Table : Effectiveness and safety
Question : How effective and safe is the Rezūm therapy for management of LUTS secondary to BPH?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
2. Rezūm II Trial a. McVary KT, Gittelman MC, Goldberg KA 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. b. Roehrborn CG, Gange SN, Gittelman MC et al. 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. J Urol. 2017;197(6):1507-1516 **(*Cross-over group results*) c. McVary KT,	Multicentre, double-blinded randomised controlled trial RCT comparing Rezum with sham with primary endpoint at 3 months (ITT analysis), when blinding was removed. Following washout at 6 months, sham patients were offered treatment with Rezum. **Setting/country**:15 sites /USA **Methods** Inclusion criteria - Males ≥ 50 years of age who had symptomatic BPH - IPSS ≥13 - Qmax between 5 and 15mL per second with a voided volume ≥ 125mL - Prostate volume 30gm to 80gm measured by transrectal ultrasound - No prior invasive prostate intervention or surgery of the prostate - Required to undergo a washout period for the following: antihistamines(1week); a-blockers, anti-cholinergics, or daily dose phosphodiesterase type 5 inhibitors (4 weeks); oestrogen, androgen sup-pressing drugs, anabolic steroid, or type II 5a-reductase inhibitors (3 months); dual 5a-	I	197 patients randomized in a 2:1 ratio (136 sham, 61 sham). Total of 188 patients from intervention and crossed over from sham. At 5 years, total of 77 patients were analysed. Rezūm group - Number of men randomised: 136 - Age in years (mean±SD):63±7.1 - Prostate volume in mls (mean±SD): 45.8±13.0 - PSA in ng/mL (mean±SD): 2.1±1.5 - IPSS (mean±SD): 22±4.8 - Qmax in mls/s(mean±SD): 9.9±2.3 - PVR in mls(mean±SD): 82±51.5 - OP time: NR Sham group - Number of men randomised: 61 - Age in years (mean±SD): 62.9±7.0 - Prostate volume in mls (mean±SD): 44.5±13.3 - PSA in ng/mls (mean±SD): 2.0±1.6 - IPSS (mean±SD): 21.9±4.7 - Qmax in mls/s (mean±SD): 10.4±2.1 - PVR in mls (mean±SD): 82±51.5 - OP time: NR	Rezūm therapy	Sham (mock procedure - rigid cystoscopy with simulated active treatment sound effects)	5 years	**IPSS** - At 3 months (McVary et al., 2016) Rezum: -11.2 (95% CI -12.5 to -9.9) Sham: -4.3 (95% CI -6.1 to -2.5). Significantly favours Rezum (p < 0.0001) -Cross over data (Roehrborn et al., 2017) Rezum: -10.0 (95% CI -12.1 to -8.0) Sham: -3.9 (95% CI -5.8 to -2.0). Significantly favours Rezum (p = 0.0004) -12 months, change of -9.4 ± 8.7; 2 years, change of -12.1 ± 7.9; 3 years, change of -11.0±7.0; 4 years, change of -10.1 ± 7.6; 5 years, change of -10.9 **IPSS-QoL** -At 3 months (McVary et al., 2016) Rezūm: -2.1 (95% CI -2.4 to -1.8) Sham: -0.9 (95% CI -1.3 to -0.5) Significantly favours Rezum (p < 0.0001) -Cross over data (Roehrborn et al., 2017) Rezum: -2.0 (95% CI -2.5 to -1.5) Sham: -0.8 (95% CI -1.2 to -0.3). Significantly favours Rezum (p = 0.0024) -12 months, change of -1.9 ± 1.8; 2 years, change of -2.0 ± 1.8; 4 years, change of -2.0 ± 1.7; 5 years, change of -2.2 **BPHII** -At 3 months (McVary et al., 2016) Rezum: -3.4 (95% CI -4.0 to -2.4) Sham: -0.9 (95% CI -2.3 to -0.7). Significantly favours Rezum (p < 0.0003) -Cross over data (Roehrborn et al., 2017) Rezum: -2.9 (95% CI -3.9 to -2.0) Sham: -1.3 (95% CI -3.1 to -0.5). Significantly favours Rezum (p = 0.00241) -2 years, change of -4.8 ± 3.5; 4 years, change of -3.5 ± 3.4. **IIEF-EF** -Cross over data (Roehrborn et al., 2017) Rezum: -0.9 (95% CI -0.9 to -2.7) Sham: -0.1 (95% CI -2.7 to 2.5). No significant difference from sham (p = 0.5972). -4 years, change of -2.5 ± 8.7 Non-significant from baseline (p =0.0333) (McVary et al., 2019).

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
Roehrborn CG. Three-Year Outcomes of the Prospective, Randomized Controlled Rezūm System Study: Convective Radiofrequency Thermal Therapy for Treatment of Lower Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia. Urology. 2018;111:1-9 d. McVary KT, Rogers T, Roehrborn CG. Rezūm Water Vapor Thermal Therapy for Lower Urinary Tract Symptoms Associated With Benign Prostatic Hyperplasia: 4-Year Results From Randomized Controlled Study. Urology. 2019;126:171-179 e. McVary KT, Gittelman MC, Goldberg KA 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	reductase inhibitors (6 months) <u>Exclusion criteria</u> - PVR >250mL - PSA > 2.5ng/mL with a free PSA <25% (unless prostate cancer was ruled out by biopsy) - An active urinary tract infection within 7days, or 2 independent infections within the last 6months **Randomisation and allocation concealment** -randomized with an electronic program before treatment using permuted blocks of random sizes, stratified by investigational sites **Blinding** -The urologist was not blinded in order to perform the treatments but did not participate in the follow-up or the administration of outcomes questionnaires -Study participants and study personnel administering questionnaires were blinded. **Analysis** **-** Intention to treat analysis for parallel group in the first 3 months follow-up -Per protocol analysis after cross-over period of sham group (during follow up period at 1, 2, 3, 4 and 5 years)						-5 years, change of -2.4 ± 9.2 (McVary et al., 2021). **MSHQ-EjD function** -Cross over data (Roehrborn et al., 2017) Rezum: -0.4 (95% CI -1.6 to 0.8) Sham: -0.6 (95% CI -0.3 to 1.4). No significant difference from sham (p = 0.2825) -4 years, change of -1.8 ± 4.4 Significant from baseline (p =0.0038) (McVary et al., 2019). -5 years, change of --2.0 ±3.9 (McVary et al., 2021). **MSHQ-EjD bother** -Cross over data (Roehrborn et al., 2017) Rezum: -0.1 (95% CI -0.6 to 0.8) Sham: -0.3 (95% CI -0.6 to 0.5). No significant difference from sham (p = 0.6778) - 4 years, change of -0.1 ± 1.8 Non-significant from baseline (p =0.6495) (McVary et al., 2019). -improvement remained consistent through the length of follow-up with a 16% improvement at 5 years (McVary et al., 2021). **Qmax** -At 3 months (McVary et al., 2016) Rezum: 6.2 (95% CI 5.0 to 7.0) Sham: 0.5 (95% CI -0.6 to 1.5) Significantly favours Rezum (p < 0.0001) - Cross over data (Roehrborn et al., 2017) Rezum reduction: 6.3 (95% CI 4.3 to 8.3) Sham reduction: 0.2 (95% CI -0.9 to 1.3) Significantly favours Rezum (p < 0.0001) - 12 months, change of 1.5 ± 5.9; 2 years, change of 3.7 ± 6.5; 4 years, change of 4.2 ± 5.7 **PVR** -At 3 months (McVary et al., 2016) Rezum: -10.6 (95% CI -22.3 to 1.1) Sham: 7.2 (95% CI -12.6 to 27.0) No significant difference (p = 0.108) - 12 months, change of -159.0 ± 254.7; 2 years, change of -15.6 ± 93.1; 4 years, change of -9.2 ± 72.2

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
Lower Urinary Tract Symptoms Secondary to Benign Prostatic Hyperplasia. J Urol. 2021;206(3):715-724	**Patient reported outcome measures and QoL outcomes**: IPSS IPSS-QoL (question 8) BPHII ICS score IIEF-EF MSHQ function MHSQ bother Clinical outcomes: Qmax PVR Reduction in prostate volume Healthcare resource use: Number catheterised Requirement for retreatment Adverse events: Device and procedure related adverse events Persistence of LUTs Dysuria Post-operative UTIs **Funding sources** NxThera Inc.						**Reduction in prostate volume** After 6 months, there is a 28.9% (17.7 cm3) reduction in whole prostate volume compared with 1- week post-procedure N**eed for and/or duration of catheterisation** 90.4% (122/135) of patients were catheterised for a mean 3.4 ± 3.2 days in the Rezum arm. **Time to daily activities** Rezum: median 4 days (range 0 to 90 days) **Rates of surgical retreatment for BPH** 2.3% after 1 year; 4.4% at 5 years **Rates of medical retreatment for BPH** 0.8% after 1 year; 11.1% at 5 years **Safety** - No perioperative device or procedure-related AEs - 8 serious AEs in 7 subjects reported at 0-3 months (5.1%), of which 3 serious AEs in 2 subjects were adjudicated as procedure- related (1.5%), comprising: 1 *de novo* extended urinary retention 1, 1 nausea and vomiting due to alprazolam - In the crossover group at 3- 12 months (n=53), 8 serious AEs reported in 6 subjects (11.3%), of which 3 serious AEs in 2 subjects were adjudicated as procedure- related (3.8%), comprising:1 subject with bladder contracture and bladder calculi 6 months after Rezūm 1 urosepsis after FU cytoscopy Rate of dysuria (pain) :16.9% Urinary frequency: 5.9% Urinary urgency: 5.9% Rate of urinary retention: De novo, extended 0.7%; acute 3.7% Urinary tract infection (UTI): Culture proven UTI 2.9%; Suspected UTI 3.7%; Epididymitis 2.9% Gross haematuria: 11.8%, Haematospermia: 7.4% Bladder neck contracture or stricture : 1.9%

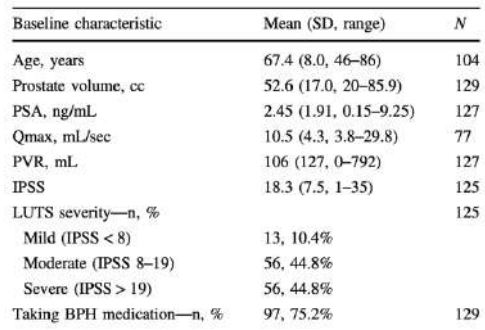
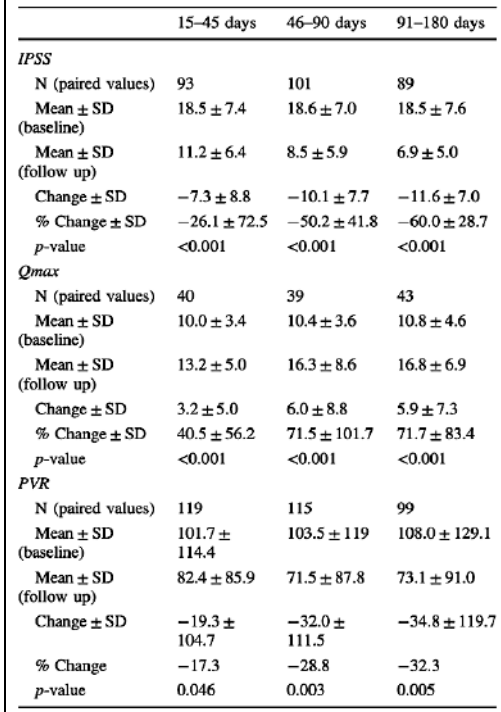
Evidence Table : Effectiveness and safety
Question : How effective and safe is the Rezūm therapy for management of LUTS secondary to BPH?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
3. Tutrone RF, Schiff W. Early patient experience following treatment with the UroLift prostatic urethral lift and Rezum steam injection. Can J Urol. 2020;27(3):10213-10219.	Prospective cohort study **Setting**: 2 centres, USA **Objective** To report the early postoperative patient experience, including symptom response, catheterization, recovery and satisfaction, following treatment with 2 MIST for BPH: mechanical disobstruction with UroLift prostatic urethral lift (PUL) and tissue ablation with steam injection (Rezum). **Inclusion criteria** Rezūm group Men ≥ 50 years old and a prostate volume ≥ 30 cc and ≤ 80 cc. UroLift group Men aged ≥ 45 and prostates ≤ 100 cc with no lower limit. No exclusion criteria were established for either modality regarding baseline symptom score, prostate size, retention history, bilobar or trilobar prostatic obstruction, or BPH medical therapy, as patients needed only to have undergone a procedure to be enrolled.	**II-2**	53 participants [UroLift (n = 30); Rezum (n = 23)] Mean age: 69 ± 8.6 y.o. (68 ± 9.4 PUL versus 69 ± 7.8 Rezum) Mean prostate volume: 56 ± 30.1 (49 ± 28.4 PUL versus 63 ± 30.9 Rezūm) Baseline IPSS scores were available for 19 PUL and 12 Rezum patients with no significant difference between groups (16 ± 7.0 PUL versus 18 ± 6.6 Rezum, p = 0.4).	Rezūm therapy	UroLift	2 months	**Symptom outcomes following treatment with Urolift or Rezūm** **Outcome measure (mean ± SD)** / **PUL (n = 30)** / **Rezum (n = 23)** / **p value** IPSS: 8.6 ± 5.0 / 15.6 ± 9.2 / 0.001 IPSS QoL: 1.5 ± 1.5 / 2.5 ± 1.9 / 0.04 SHIM: 14.8 ± 8.6 / 9.2 ± 7.2 / 0.02 MSHQ-EjD: 12.2 ± 2.7 / 9.2 ± 5.1 / 0.04 MSHQ-EjD bother: 1.1 ± 1.4 / 1.5 ± 1.6 / 0.4 % BPH medication usage: 37% / 91% / < 0.0001 % new BPH medication usage: 10% / 17% / 0.5 IPSS = International Prostate Symptom Score; QoL = quality of life; SHIM = Sexual Health Inventory for Men; MSHQ-EjD = Male Sexual Health Questionnaire-ejaculatory dysfunction; BPH = benign prostatic hyperplasia - Absolute IPSS scores for all available patients (PUL n = 29, Rezum n = 22) were significantly better for PUL as compared to Rezum - QoL scores aligned with IPSS differences, with patients who underwent PUL indicating significantly better quality of life (1.5 ± 1.5) than those who received Rezum (2.5 ± 1.9) (p = 0.04) - Overall measurements for MSHQ-EjD were significantly better in PUL patients (12.2 ± 2.7 versus 9.2 ± 5.1, respectively, p = 0.04), as PUL patients reported the ability to ejaculate more often during sexual activity and trended towards better outcomes in volume of ejaculate. MSHQ-EjD bother score was not different between treatments. **Catheterization** -Rate of postoperative catheterization was significantly different between treatment groups: 57% of UroLift patients and 87% of Rezum patients were catheterized after undergoing their procedure (p = 0.03) - Duration of catheterization differed significantly between UroLift and Rezum patients. The mean duration for all UroLift patients was 1.2 ± 2.3 days whereas Rezum patients were catheterized for an average of 4.5 ± 3.8 days (p = 0.0004)

	Outcome measures Urinary symptoms (IPSS and IPSS QoL), urinary catheter experience, recovery and interference with daily activities, BPH medication use, treatment satisfaction, and sexual function (MSHQ-EjD).						- 7% of PUL patients were still catheterized by postoperative day 3 compared to 55% of Rezum patients (p = 0.0003) **BPH medication use** -Rate of medication use within 2 months post procedure (either alpha-blocker or 5-ARI) after procedure was 37% for PUL and 91% for Rezum patients (p = < 0.0001) - *De novo* medication use reported as a new prescription following the procedure, was 10% for PUL patients and 17% for Rezum patients (p = 0.5). **Recovery** - 40% of Rezum patients reported interference at least "some of the time" from entertainment related activities, i.e., going to movies, shows, spectator sports, and cultural events, compared to 8% of PUL patients (p = 0.01) - 40% and 50% of Rezum patients (versus 12% and 0% of PUL patients, p = 0.04 and p = 0.007) reported interference with community-related activities, i.e., volunteering, attending church, cultural activities, visiting with family, and sports-related activities, respectively **Satisfaction** -97% PUL patients rated their urinary symptoms as being at least "a little better" (97%), which is significantly different from the 70% of Rezum patients who met the same criteria (p = 0.02) - Patients' satisfaction of procedure on their voiding symptoms, with 22% of Rezum versus 3% of UroLift patients (p = 0.07) - 26% of Rezum patients reported being dissatisfied or worse with their recovery versus 7% of UroLift patients - General satisfaction score: UroLift patients were more satisfied than Rezum patients, with a score of 2.5 versus 1.4 (p = 0.08). **Conclusion** Short term outcome of 2 months showed that both treatments alleviate bothersome LUTS, however UroLift PUL provided more rapid recovery with a lower rate of postoperative catherization, which may be reflected in higher treatment satisfaction

							compared with Rezum.

Evidence Table : Effectiveness and safety
Question : How effective and safe is the Rezūm therapy for management of LUTS secondary to BPH?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
4. Mollengarden D, Goldberg K, Wong D et al. Convective radiofrequency water vapor thermal therapy for benign prostatic hyperplasia: a single office experience. Prostate Cancer Prostatic Dis. 2018;21(3):379-385.	Retrospective cohort study **Setting**: single centre, USA **Inclusion criteria** -all patients who underwent the Rezūm procedure by a single surgeon in an office of the Urology Department at UT Southwestern Medical Center - at least 4 months out from treatment. **Outcome measures** IPSS, Qmax, PVR, adverse events and satisfaction level	**II-2**	129 participants **Baseline characteristics** 	Rezūm therapy	No comparator	6 months	**Mean changes in IPSS, Qmax and PVR post operatively**  - Significant improvements in IPSS, Qmax, and PVRs from baseline over all evaluated time intervals with the greatest improvements at 3–6 months from procedure - 11.6 point improvement in IPSS at the 3-6 months interval. Benefits were greater for voiding symptoms (73.6% reduction) than storage

Baseline characteristic	Mean (SD, range)	N
Age, years	67.4 (8.0, 46–86)	104
Prostate volume, cc	52.6 (17.0, 20–85.9)	129
PSA, ng/mL	2.45 (1.91, 0.15–9.25)	127
Qmax, mL/sec	10.5 (4.3, 3.8–29.8)	77
PVR, mL	106 (127, 0–792)	127
IPSS	18.3 (7.5, 1–35)	125
LUTS severity—n, %		125
Mild (IPSS < 8)	13, 10.4%	
Moderate (IPSS 8–19)	56, 44.8%	
Severe (IPSS > 19)	56, 44.8%	
Taking BPH medication—n, %	97, 75.2%	129

	15–45 days	46–90 days	91–180 days
IPSS			
N (paired values)	93	101	89
Mean ± SD (baseline)	18.5 ± 7.4	18.6 ± 7.0	18.5 ± 7.6
Mean ± SD (follow up)	11.2 ± 6.4	8.5 ± 5.9	6.9 ± 5.0
Change ± SD	−7.3 ± 8.8	−10.1 ± 7.7	−11.6 ± 7.0
% Change ± SD	−26.1 ± 72.5	−50.2 ± 41.8	−60.0 ± 28.7
p-value	<0.001	<0.001	<0.001
Qmax			
N (paired values)	40	39	43
Mean ± SD (baseline)	10.0 ± 3.4	10.4 ± 3.6	10.8 ± 4.6
Mean ± SD (follow up)	13.2 ± 5.0	16.3 ± 8.6	16.8 ± 6.9
Change ± SD	3.2 ± 5.0	6.0 ± 8.8	5.9 ± 7.3
% Change ± SD	40.5 ± 56.2	71.5 ± 101.7	71.7 ± 83.4
p-value	<0.001	<0.001	<0.001
PVR			
N (paired values)	119	115	99
Mean ± SD (baseline)	101.7 ± 114.4	103.5 ± 119	108.0 ± 129.1
Mean ± SD (follow up)	82.4 ± 85.9	71.5 ± 87.8	73.1 ± 91.0
Change ± SD	−19.3 ± 104.7	−32.0 ± 111.5	−34.8 ± 119.7
% Change	−17.3	−28.8	−32.3
p-value	0.046	0.003	0.005

symptoms (48.6% reduction).
-Qmax improved from a baseline average of 10.5 mL/s to 16.8 mL/s at 3-6 months.
- Of the patients who were on an alpha blocker and/or 5- alpha reductase inhibitor preoperatively, 89.5% (85/95) were off all medications at their latest follow up.

Adverse events

			Clavien-Dindo classification				
Adverse events	*n*	%	I	II	III	IV	V
UTI	22	17.1	0	22	0	0	0
Spanner patients	13	23.1					
Catheter patients	9	14.4					
Cystoscopic LUTS evaluation	10	7.8	0	0	10	0	0
Urinary retention	18	14.0	16	0	2	0	0
from blood clots	4	3.1					
from UTI	1	0.8					
from prostate edema	13	10.1					
Urethral stricture	5	3.9	0	0	5	0	0
Postvoid dribbling	5	3.9	5	0	0	0	0
Urinary incontinence	5	3.9	5	0	0	0	0
Erectile dysfunction	4	3.1	3	2	0	0	0
Retrograde ejaculation	4	3.1	4	0	0	0	0
Additional BPH surgery	3	2.3	0	0	3	0	0
Prostate tissue sloughing	2	1.6	2	0	0	0	0
Epididymo-orchitis	2	1.6	0	2	0	0	0
Bladder stone	1	0.8	0	0	1	0	0
Bladder neck contracture	1	0.8	0	0	1	0	0

Satisfaction level
- Mean procedural satisfaction was 4.2 out of 5. In total 59% were very satisfied, 18% satisfied, 10% neutral, 8% dissatisfied, and 6% very dissatisfied.
- Mean result satisfaction was 4.0 out of 5. In total 40% were very satisfied, 25% satisfied, 14% neutral, 4% dissatisfied, and 10% very dissatisfied.
- 86% of patients would recommend the procedure to a friend in similar circumstances.

Conclusion
Rezūm therapy resulted in improvement of urologic symptoms with a reasonable side effect profile. There is a notable rate of early

							postoperative urinary retention which patients should be aware of.

Evidence Table : Effectiveness and safety
Question : How effective and safe is the Rezūm therapy for management of LUTS secondary to BPH?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
5. Siena G, Cindolo L, Ferrari G et al. Water vapor therapy (Rezūm) for lower urinary tract symptoms related to benign prostatic hyperplasia: early results from the first Italian multicentric study. World J Urol. 2021:1-6.	Prospective cohort study **Setting**: 5 sites, Italy **Objective** - Aim to carefully assess the functional outcomes of patients treated with Rezūm for BPH. **Inclusion criteria** -age > 18, no prior prostate interventions, IPSS ≥ 13, post-void residual ≤ 250 mL, prostate volume between 30 and 120 cc **Outcome measures** -IPSS, International Consultation on Incontinence Questionnaire-Short Form (ICIQ-UI SF), the Overactive Bladder Questionnaire-Short Form (OAB-q SF) score, the International Index of Erectile Function (IIEF-5) and questions 9 and 10 to assess ejaculatory dysfunction	**II-2**	**135 participants** **Baseline characteristics** Age (years), median IQR: 69 (61–79) BMI (kg/m2), median IQR: 24 (22.8–26) Median PSA :2.1 (1.3–4.0) ng/ mL Median PV: 60 (45–78) mL Preoperative median Qmax: 8.1 (6–10) Preoperative median Qmed : 3.7 (2.1–6.2) Preoperative medical treatment for BPH [*n*. %] : Alpha-blocker 48.9% 5-ARI 3% Phytotherapic 3% Alpha-blocker, 5-ARI phytotherapic 17% Alpha-blocker, 5-ARI 24.4% Alpha blocker, phytotherapic 3% Anticholinergic 0.74% Baseline median IPSS: 21.5 (17–25) Baseline median OAB-q SF: 33 (19–52) Baseline median IIEF-5 score : 21.5 (17–25).	Rezūm therapy -The use and type of anesthesia were variable from oral sedation to prostate block, intravenous sedation or mild general anesthesia in accordance with local protocol and patients' preferences -Antibiotics were administered to all patients according to local practice guidelines. Prophylaxis included either Quinolones (Levofloxacin 500 mg once daily for 7 days) or Cephalosporine 400 mg daily for 7 days	No comparator	1, 3 and 6 months	- Median operative time from the instrument tran-surethral insertion to patient catheterization was 10.5 (IQR 8.7–15.0) minutes. - Patients received a median of 7 (IQR 5–8) PEEK vapour needle injections - All patients were dismissed few hours after surgery with indwelling urinary catheter that was removed after a median of 7 (IQR 7–10) days. Postoperative outcomes (*n* = 135) Postoperative acute urinary retention [*n*. %] 16 11.8% Day of urinary catheter removal (median IQR) 7 7–10 1st month IPSS score (median IQR) 7.5 5–12 3rd month IPSS score (median IQR) 4.2 3.2–5.3 6th month IPSS score (median IQR) 4.4 3.8–5.9 1st month OAB-q SF score (median IQR) 16.5 13–3.-23.7 3rd month OAB-q SF score (median IQR) 16 14.5–16.4 3rd month IIEF-5 score (median IQR) 12.5 0.7–21.7 6th month IIEF-5 score (median IQR) 23.5 21–25.5 -A significantly decrease of IPSS from baseline at first [21.5 (IQR 17–25) vs 7.5 (5–12.), *p* = 0.001], third [21.5 vs 4.2 (IQR 3.2–5.3), *p* < 0.0001] and sixth [21.5 vs 4.4 (IQR 3.8–5.9), *p* < 0.0001] months after surgery - No difference was reported in terms of ICIQ-UI SF score post- operatively. -A mild reduction of the OAB-q SF score was reported at 1 month from surgery [33 (IQR 19–52) vs 16.5 (13.3–23.7), *p* = 0.06] that turned significant at 3 months postoperatively [33 vs 13 (IQR 12.5–16.4), *p* < 0.0001]. -A slight but statistically significant increase of the IIEF-5 score was reported from baseline at 6 months [20 vs 23.5 (IQR 21–25.5), *p* = 0.04].

							Adverse events -Complication rate was 48%, all CDC grade 1 -Complications were: mild hematuria, hematospermia, dysuria, urinary tract infections (UTI) and AUR. Mild hematuria, hematospermia and dysuria were self-limiting within maximum 6 weeks. UTI (6%), acute urinary retention (11.8%) **Sexual dysfunction** - 2% of retrograde ejaculation - no de novo erectile dysfunction

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Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
6. Johnston MJ, Noureldin M, Abdelmotagly Y et al. Rezum water vapour therapy: promising early outcomes from the first UK series. BJU Int. 2020;126(5):557-558.	Prospective cohort study **Setting:** Single centre, UK Inclusion and exclusion were not reported **Outcome measures** IPSS, QoL, IIEF, PVR, Qmax	**II-2**	210 participants **Baseline characteristics** Mean age: 66 years old Mean Qmax, mL/s: 9.2 Mean PVR, mL :170.9 Mean Prostate volume, mL: 56.9 Mean IPSS: 20.4 Mean QoL score : 4.3 Mean IIEF-5 score: 15.2	Rezūm therapy	No comparator	1 year	- Both the IPSS and quality-of- life (QoL) score improved significantly from baseline to 3, 6 and 12 months (all P < 0.001).

Variable	Baseline	3 months	6 months	12 months
Q_{max}, mL/s	9.2	15.8	15.2	18.1
PVR, mL	170.9	100	96.5	108
Prostate volume, mL	56.9	38.1		
IPSS	20.4	5.9	5.5	4.3
QoL score	4.3	1.4	1.3	1.2
IIEF-5 score	15.2	17.7	16.8	20.6

Adverse events
- 6% UTI requiring antibiotics (one requiring hospitalisation)
-one man suffering persistent prostatitis (Clavien–Dindo Grade II).
- 2 patients required a return to theatre, both for secondary haemorrhage requiring bladder washout at 6 weeks after treatment (Clavien–Dindo Grade IIIb), and another two underwent a second procedure within the first year due to persistent or deteriorating symptoms.

Sexual function
-The erectile function scores (IIEF-5questionnaire) also improved significantly at 3, 6 and 12 months (P = 0.001).
-There were no cases of de novo erectile dysfunction.
-Six men reported de novo dry ejaculation after the procedure

Satisfaction level
- at 6 months, 191 men (91%) reported that they would go through a Rezum procedure again, should the need arise, and 186 men (89%) rated their satisfaction with the procedure as either

							'satisfied' or 'very satisfied'.

Evidence Table : Effectiveness and safety
Question : How effective and safe is the Rezūm therapy for management of LUTS secondary to BPH?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
7. Darson MF, Alexander EE, Schiffman ZJ et al. Procedural techniques and multicenter postmarket experience using minimally invasive convective radiofrequency thermal therapy with Rezūm system for treatment of lower urinary tract symptoms due to benign prostatic hyperplasia. Res Rep Urol. 2017;9:159-168.	Retrospective cohort (post marketing study) **Setting**: 2 large group-community practices, USA **Objective:** To evaluates clinical experience with the Rezūm system after US Food and Drug Administration clearance in consecutive cases accrued by multiple community urologists for the treatment of LUTS associated with BPH. Patients recruited consecutively with data collected at baseline, 1 month, 3 to 6 months, and 12 months. Subgroup analysis was performed based on symptom severity (moderate LUTS and severe LUTS) **Inclusion criteria:** Men with bothersome LUTS due to BPH treated with Rezūm convective RF thermal therapy No exclusion criteria	**II-2**	131 participants **Baseline characteristics** Mean age, years : 70.9 (9.4) Mean prostate volume (mls): 45.1 (23.4) Mean PSA (ng/mL): 3.5 (5.6) Mean Qmax (mL/s): 8.6 (4.9) Mean PVR volume (mL): 216.8 (286.6) Mean IPSS: 19.5 (6.6) **LUTS severity** Moderate: 53.1% Severe: 46.9%	Rezūm therapy - perfomed by multiple urologists - type of anaesthesia: intravenous sedation or prostate block followed by posttreatment analgesics [intravenous sedation (86%), general anaesthesia (15%), or prostate block (6%)].	No comparator	1 year	-Significant relief of LUTS was observed with baseline IPSS reduced by 16%, 47%, and 45% at the three time-point, respectively (P<0.0001). Mean baseline IPSS of 19.5 decreased an average of 10.1 and 9.4 points at 3–6 months and 12 months. -Significant improve- ments in QOL and PVR volume were commensurate with IPSS improvements.

Outcome measure	Baseline	1 month	3–6 months	12 months
IPSS				
n (paired values)	128	93	115	87
Baseline	19.5 (6.6)	19.9 (6.5)	19.9 (6.7)	19.4 (6.7)
Follow-up		16 (8)	9.8 (6.9)	10.1 (7.2)
Change		−3.9 (8.2)	−10.1 (8.8)	−9.4 (8.7)
% change		−15.9	−47.2	−45.2
P-value (GEE)		<0.0001	<0.0001	<0.0001
QOL (IPSS question 8)				
n (paired values)	112	81	104	74
Baseline	4.3 (1.2)	4.4 (1.2)	4.3 (1.2)	4.4 (1.3)
Follow-up		3.7 (1.8)	2.3 (1.5)	2.5 (1.4)
Change		−0.6 (1.9)	−2 (1.7)	−1.9 (1.8)
% change		−7.2	−42.7	−37.8
P-value (GEE)		0.0007	<0.0001	<.00001
Q_{max} (mL/second)				
n (paired values)	94	23	38	7
Baseline	8.6 (4.9)	8.3 (3.8)	8.7 (4.7)	8.5 (3.5)
Follow-up		9.6 (5.9)	11.6 (7.7)	10 (5)
Change		1.3 (5.1)	3 (9)	1.5 (5.9)
% change		20.7	75.3	51.4
P-value (GEE)		0.2047	0.0388	0.4257
PVR volume (mL)				
n (paired values)	115	83	89	35
Baseline	216.8 (286.6)	209.9 (273.5)	243.8 (316.7)	236.6 (341.3)
Follow-up		82.5 (144.2)	85.8 (167.3)	77.3 (122.1)
Change		−127 (257.1)	−158 (221.8)	−159 (254.7)
% change		44.6	−30.2	−34.9
P-value (GEE)		<0.0001	<0.0001	<0.0001
Voided volume (mL)				
n (paired values)	94	25	38	7
Baseline	163.2 (108.4)	165.4 (122.8)	192.3 (119.4)	182.7 (119.4)
Follow-up		114.6 (77.3)	146.7 (100.6)	138.4 (103.1)
Change		−50.8 (133.9)	−45.5 (149.8)	−44.2 (146.6)
% change		12.9	30.9	0.5
P-value (GEE)		0.0377	0.1948	0.5129

Adverse events

	Outcome measures Patient reported outcome and QoL outcomes IPSS IPSS-QoL Clinical outcomes Qmax,PVR Voided volume						**-**No perioperative device or procedure-related AEs -AEs were mild–moderate in severity, and most resolved within a short time after routine treatment or without treatment (acute urinary retention 10.7%;urinary frequency, urgency, frequency and urgency, hematuria, and nocturia in ≤3.8%) -2% of patients with obstructing residual tissue or insufficient improvement underwent a TURP procedure 7–12 months later; one patient had a second Rezūm procedure 12 months later.

Evidence Table : Effectiveness and safety
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Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
8. 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):405-413	Retrospective cohort study **Setting:** Rezum group-15 sites; medical therapy group-17 sites, USA (Data drawn from 2 RCTs) **Objective** To conduct evaluation of the long-term treatment outcomes for LUTS/BPH, comparing the one-time application of Rezum therapy procedure to daily medical therapy in the treatment cohorts of the MTOPS study **Eligibilty criteria** men aged at least 50 years old, PV 30 to 80 mls, IPSS ≥13, Qmax ≤15 mL/s, PVR≥ 125 mL. **Outcome measures** changes over time in IPSS, BPHII, Qmax, and PVR, as well as clinical progression of BPH	**II-2**	1275 (Rezum-129/ Doxazosin-368/Finasteride-394/ Combo-384) *(propensity matching)* Mean age, years: Rezūm - 63.3 ± 7.0 Doxazosin - 62.4 ± 7.3 Finasteride - 63.1 ± 7.2 Combo – 62.6 ± 6.3 Mean baseline prostate size: Rezum -46.0 ± 13.1 Doxazosin - 39.3 ± 10.1 Finasteride - 38.0 ± 8.9 Combo – 37.7 ± 9.5 Mean baseline IPSS Rezum - 21.5 ± 4.3 Doxazosin - 21.4 ± 4.3 Finasteride - 21.4 ± 4.2 Combo – 21.2 ± 3.9 Mean baseline IPSS-QoL Rezum - 4.4 ± 1.0 Doxazosin - 4.3 ± 1.0 Finasteride - 4.3 ± 1.0 Combo – 4.5 ± 1.0 Mean baseline BPHII Rezum - 6.2 ± 2.8 Doxazosin - 5.6 ± 2.3 Finasteride - 6.2 ± 2.7 Combo – 6.1 ± 2.5 Mean baseline Qmax Rezum - 9.9 ± 2.3 Doxazosin - 9.9 ± 2.3 Finasteride - 10.3 ± 2.3 Combo – 10.2 ± 2.4	Rezūm therapy	Medical therapy	3 years	**Clinical progression of BPH** **-** The rate of BPH clinical progression among subjects treated with either with doxazosin, finasteride or combination thermal therapy was 1.5 to 1.7 per 100 person-year compared with 0.3 per 100 person-year for Rezuml therapy subjects **Urologic symptoms and QoL** -A single procedure with Rezum therapy resulted in a significantly greater mean [95% CI] improvement in IPSS from baseline at 3 months as compared with the 3-month improvement with doxazosin (Δ=2.6 [1.2, 3.9] p<0.001) or finasteride (Δ=5.2 [4.0, 6.4] p<0.001). -IPSS improvements with Rezūm therapy remained durable throughout 36 months, whereas continued use of doxazosin or finasteride showed little further I-PSS improvement over 36 months and remained significantly less than for Rezum therapy (Δ=1.8 [0.4, 3.2] p=0.02 and Δ=2.2 [1.0, 3.4] p<0.001). -The combination drug cohort had similar IPSS improvements at 3 months compared to Rezūm therapy (Δ=1.4 [0, 2.8] p=0.05); outcomes were better on average for thermal therapy at 6 and 12 months (p=0.02 and p=0.03) followed by similar significant improvements from baseline through 36 months. -Significant improvement in the BPHII quality of life measure after Rezum therapy compared to doxazosin at each visit over 36 months (p=0.02 to p<0.001), and finasteride over 24 months (p=0.03 to p<0.001). -Treatment with Rezum therapy compared with continued use of doxazosin resulted in significantly greater improved peak flow rates over 3 to 12 months (p=0.01 to p=0.03) and greater improvements throughout 36 months compared with finasteride, (p<0.001 to p=0.002). -Similarly, Rezum therapy significantly improved

							Qmax for up to 12 months compared with combination drug therapy (p<0.001 to p=0.002)..

Evidence Table : Effectiveness and safety
Question : How effective and safe is the Rezūm therapy for management of LUTS secondary to BPH (Prostate volume ≥ 80mls)?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
9. Bole R, Gopalakrishna A, Kuang R et al. Comparative Postoperative Outcomes of Rezūm Prostate Ablation in Patients with Large Versus Small Glands. J Endourol. 2020;34(7):778-781.	Retrospective cohort study **Setting**: single centre, USA **Objective:** To determine the efficacy of Rezūm in men with BPH-related LUTS and gland size >80cc via a single institution retrospective review. Inclusion and exclusion criteria not reported **Outcome measure** Pre- and 3 month post-procedural AUA symptom score, Qmax, and post-void residual (PVR)	**II-2**	182 participants [Large prostates (LP): n=47; small prostates(SP): n=135] Mean age: LP-72(10); SP-69(9) Prostate volume: LP-119(26); SP- 49(18)	Rezūm therapy for large prostates (≥80mls)	Rezūm therapy for small prostates (<80mls)	3 months	-Statistically significant improvement was seen in IPSS from 22 to 13.4 (p=0.04) and PVR from 305mls to 149mls (0.05). -Statistically significant improvement was seen in peak flow rate from 7.7 mL/second to 12.7 mL/second (p=0.002).

Outcome variables	Gland < 80 g Mean	*p*-value	Large gland Mean	*p*-value
AUA symptom Score (SD)				
Pre-op	22.1 (6.0)	0.0005	22.0 (5.3)	0.04
Post-op	12.1 (5.4)		13.4 (6.7)	
Peak flow, mL/sec (SD)				
Pre-op	9.2 (4.5)	0.001	7.7 (3.8)	0.002
Post-op	12.9 (6.8)		12.7 (8.7)	
Post-Void Residual, mL (SD)				
Pre-op	301 (252)	<0.001	305 (209)	0.05
Post-op	157 (135)		149 (132)	

Adverse events
- Postoperative complication rate was not significantly different between large or small glands.

Complications	Gland < 80 g (N = 135)	Large gland (N = 47)	*p*-value
Catheter irrigation	7 (5.2%)	7 (14.9%)	0.06
Cystoscopic clot evacuation	1 (0.7%)	2 (4.3%)	0.17
Transfusion	0	2 (4.3%)	0.07
Urinary Tract Infection	21 (15.6%)	4 (8.5%)	0.33
• Required inpatient admission for IV antibiotics	4 (3.0%)	1 (2.1%)	0.72

Evidence Table : Effectiveness and safety
Question : How effective and safe is the Rezūm therapy for management of LUTS secondary to BPH (Prostate volume ≥ 80mls)?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
10. Garden EB, Shukla D, Ravivarapu KT et al. Rezum therapy for patients with large prostates (≥ 80 g): initial clinical experience and postoperative outcomes. World J Urol. 2021;39(8):3041-3048.	Retrospective cohort **Setting**: single centre, USA **Eligibility criteria** Patients who underwent Rezum between Jan 2017–Feb 2020 Details of inclusion and exclusion criteria not reported **Outcome measures** AUA-Symptom Score (AUA- SS), Sexual Health Inventory for Men (SHIM) questionnaire score, Qmax, PVR, and total PSA levels. Clinical outcomes included trial void evaluation (TOV), nausea, vomiting, fever, hematuria, hematospermia, urgency, frequency, AUR, clot retention, bladder spasms, erectile dysfunction, UTI, and details of emergency department (ED) visits and/or readmissions within 90 days.	**II_2**	204 participants [Large prostates (LP): n=36; small prostates(SP): n=168] Mean age: LP- 67.31 (7.17); SP- 65.41 (9.05) Mean BMI: LP- 26.23 (3.42); SP-27.71 (5.21) Mean prostate volume: LP-106.77 (37.57); SP- 45.33 (14.53)	Rezūm therapy for large prostates (≥80mls)	Rezūm therapy for small prostates (<80mls)	1 year	**Perioperative data** -LP men, on average, received more total (LP 9.61, SP 4.76, p = 5.30E-13) and median lobe injections (LP 2.06, SP 1.14, p = 1.04) - Four LP procedures surpassed the standard 15 maximum treatments (16, 16, 17, and 18 injections). **Clinical outcomes** - LP men showed significant improvements in postoperative measurement of Qmax (7.39–14.60, p = 0.039) and PVR (161.09–80.85, p = 0.009), but not in AUA-SS (15.22–12.46, p = 0.29) nor SHIM (14.00–12.80, p = 0.825). -In contrast, SP men showed improved PVR (89.51–62.72, p = 0.027) and AUA-SS (16.59–11.21, p = 0.003), but not in Qmax (9.47–10.90, p = 0.187). -Longitudinally, both cohorts showed significant improvements in all clinical metrics of disease, including Qmax (LP: + 11.46, p = 0.001; SP: + 1.86, p = 0.025), PVR (LP: − 78.73, p = 0.001; SP: − 28.52, p = 0.001), and AUA-SS (LP: − 7.71, p = 0.027; SP: − 3.31, p = 0.013). - when comparing longitudinal improvements head-to-head, changes in Qmax and PVR were significantly more profound for LP men (p = 0.004 and 0.024, respectively), while average longitudinal changes in AUA-SS were not significantly different between groups (p = 0.296). -overall and longitudinal SHIM scores was hindered by limited data. -25% of LP men and 8.3% of SP men with postoperative imaging, prostate size decreased by 10.4 and 14%, respectively, though these were statistically insignificant (LP: p = 0.779, SP: p = 0.333).

							- Both cohorts significantly decreased alpha-blocker (AB) usage postoperatively (LP: 94.44–61.11%; SP: 73.96–46.15%, both p = 0.001), with insignificant changes in 5-alpha reductase inhibitor (5ARi) and phosphodiesteriase-5 inhibitor (PDE5i) use **Adverse events** -Urgency (LP: 50.00%, SP: 30.36%, p = 0.024) -No differences in rates of minor postoperative complications within one month of surgery. Both groups exhibited similar rates of postoperative UTIs, ED visits, and readmissions within 90 days; however, sub-analysis of urosepsis- related readmissions found statistically significant differences between groups (LP: 5.56%, SP: 0.00%, p = 0.002). -Neither group visited the ED (LP: POD 7.75 vs. SP: POD 16.4, p = 0.379) or was readmitted (LP: POD 8 vs. SP: POD 30.5, p = 0.309) sooner, and differences in readmission lengths were similarly insignificant (LP: 2.67 vs. SP: 5.50 days, p = 0.729). -Neither group experienced a Clavien grade ≥ III complication. **Retreatment** The difference in mean time to retreatment was statistically insignificant between groups (LP 367 days, SP 364 days, p = 0.909).

Evidence Table : Effectiveness and safety
Question : How effective and safe is the Rezūm therapy for management of LUTS secondary to BPH?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
11. Dixon CM, Cedano ER, Pacik D et al. Two-year results after convective radiofrequency water vapor thermal therapy of symptomatic benign prostatic hyperplasia. Res Rep Urol. 2016;8:207-216. The study was funded by NxThera, Inc., Maple Grove, MN, USA.	Before and after study (pilot study- proof of concept study) **Setting**: 3 international centres in the Dominican Republic, Czech Republic, and Sweden **Objective**: To assess the effectiveness and safety of Rezūm therapy in men with LUTS associated with BPH **Inclusion criteria** Men with moderate to severe LUTS secondary to BPH, age ≥45 years, IPSS ≥15, Qmax ≤15 ml/sec PVR <300 ml, Prostate volume: 20 to 120 ml **Exclusion criteria** Confirmed or suspected prostate or bladder cancer and active urinary tract infection or bacterial prostatitis within the last year Eligible participants underwent washout of antihistamines, antispasmodics (1 week; except with documented	**II-3**	65 participants **Characteristic** / **Mean (SD, range)** / **N** Age, years — 66.6 (7.7, 50.0–90.0) — 65 Prostate volume, cc — 48.6 (20. 5, 19.5–110.4) — 65 PSA, ng/mL — 3.9 (4.2, 0.2–20.3) — 65 IPSS* – all subjects — 21.6 (5.5, 13.0–35.0) — 65 LUTS severity, n (%) [range] — — 65 Moderate (IPSS ≤18) [13–18] — 21/65 (32.3%) Severe (IPSS ≥19) [19–35] — 44/65 (67.7%) QOL (question 8 of IPSS) — 4.3 (1.1, 0.0–6.0) — 65 BPHII — 6.8 (2.8, 0.0–13.0) — 64 Q_{max}, mL/s — 7.9 (3.2, 1.4–15.0) — 65 PVR, mL — 92.4 (77.3, 0.0–300.0) — 63 Ethnicity, n (%) — — 65 Caucasian — 46/65 (70.8%) Black or African origin — 2/65 (3.1%) Hispanic or Latino — 17/65 (26.2%) History of ED, n (%) — 24/50 (48.0%) — 50 History of retrograde ejaculation — 4/50 (8.0%) — 50 IIEF-15 – all subjects (total score range 0–75) — 34.4 (25.4, 5.0–73.0) — 61 IIEF-erectile function, severity score [range], n (%) — — 64 Normal [≥26–30] — 19/64 (29.7%) Mild [17≤IIEF-EF≤25] — 9/64 (14.1%) Moderate [11≤IIEF-EF≤16] — 5/64 (7.8%) Severe [1≤IIEF-EF≤10] — 31/64 (48.4%) IIEF-question 9 (score range 0–5) "When you had sexual stimulation or intercourse, how often did you ejaculate?" — — — Continuous (all subjects' scores) — 2.2 (2.3, 0.0–5.0) — 65 No sexual stimulation — 29/65 (44.6%) Almost never or never — 2/65 (3.1%) A few times (much less than half the time) — 6/65 (9.2%) Sometimes (about half the time) — 2/65 (3.1%) Most times (much more than half the time) — 5/65 (7.7%) Almost always or always — 21/65 (32.3%) MSQH-EjD function (score range 0–15) — 5.9 (4.8, 1.0–13.0) — 14† MSQH-EjD bother (score range 0–5) — 2.3 (2.3, 0.0–5.0) — 14†	Rezūm therapy	No comparator	2 years	**Perioperative data** -Mean total number of water vapor injections to lateral lobes was 4.6 (range, 2–9 injections). The median lobe was treated in 14 patients with a mean of 1.8 water vapor injections (range, 1–3 injections). -pain and anxiety management based on their clinical judgment and standard of practice. 78.5% received oral medications only for sedation and 20.9% had intravenous sedation. -Median duration of post-operative catheter use was 4.1 days **Functional urinary and QoL outcomes** - significant clinically and statistically improvements in IPSS, QOL, BPHII, and Qmax throughout the course of the 2-year study - significant reduction of −6.5 points in IPSS was achieved as early as at 1 month, *P*<0.001; the mean change of −12.5 points (56%) at 12 months was durable at the same magnitude through 24 months, −12.1 points (55% reduction), *p*<0.001. - Qmax showed incremental improvements, increasing significantly from a mean (SD) of 8.1 (3.1) mL/s at baseline to 12.7 (6.3) mL/at 12 months (*P*<0.001), and the increase remained consistent at 12.0 (6.2) mL/s at 24 months (*p*=0.001). - QOL and BPHII significantly improved and reflected improvements in LUTS in these subjects **Sexual function** No clinically significant changes in sexual function were observed over the 2-year assessments. At

	evidence of stable dosing for last 6 months), α-blockers, androgens, gonadotropin-releasing hormone analogs (2 weeks), 5α-reductase inhibitors (6 months), and use of antidepressants, anticholinergics, anticonvulsants, ß-blockers (unless with documented evidence of stable dosing). Self-administered questionnaires were given prior to the procedure and at follow-up visits conducted at 1 week, 1, 3, 6, 12, and 24 months after Rezūm therapy. **Outcome measures** <u>Patient reported and QoL outcomes</u> IPSS IPSS-QoL BPHII IIEF-EF MSHQ function MSHQ bother <u>Clinical outcomes</u> Qmax PVR Reduction in prostate volume <u>Adverse events:</u> Device and procedure related adverse events Persistence of LUTs Dysuria Post-operative UTIs.							baseline, 29.7% of patients had erectile function (IIEF-EF) scores in the normal range (≥26–30). **Safety** - 125 non-serious events reported in 45 patients. - 75% of events were reported within the first 30 days after the procedure. They were mild to moderate transient events, Clavien–Dindo class I or II, including urinary retention, dysuria, urgency, hematospermia, and suspected urinary tract infection (UTI) that resolved within a few days to 4 weeks. - 14 unrelated, serious AEs were reported in 9 patients. One patient had persistent LUTS (poor stream, frequency, and urinary retention) adjudicated as 3 separate device/procedure related grade IIIb events; the median lobe had not been treated. - No treatment related *de novo* erectile dysfunction was reported throughout the 2-year follow-up.

Events in months post procedure

AEs	Events* n	Patients N (%)	0–1 months	>1–3 months n	>3–12 months n	>12–24 months n
Serious AEs related	3	1 (1.5)	1	0	0	0
Serious AEs unrelated	14	9 (13.8)	4	1	6	3
Related non-serious AE						
Urinary retention	24	22 (33.8)	21	2	1	0
Dysuria	14	14 (21.5)	9	4	1	0
Urinary urgency	14	13 (20.0)	10	4	0	0
UTI suspected	13	13 (20.0)	8	4	1	0
Hematuria	10	9 (13.8)	10	0	0	0
Poor stream	10	9 (13.8)	6	3	1	0
Painful/discomfort – other	7	7 (10.8)	5	2	0	0
Nocturia	6	5 (7.7)	5	1	0	0
Urinary frequency	5	4 (6.2)	4	1	0	0
Urethral secretion – without hematuria or stones	3	3 (4.6)	2	0	1	0
Fever	3	3 (4.6)	3	0	0	0
Terminal dribbling	2	2 (3.1)	1	0	1	0
Scrotal pain/discomfort	2	2 (3.1)	1	1	0	0
Urinary incontinence – urge	2	1 (1.5)	1	0	0	0

Evidence Table : Effectiveness and safety
Question : How effective and safe is the Rezūm therapy for management of LUTS secondary to BPH?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
12. Alegorides C, Fourmarier M, Eghazarian C et al. Treatment of benign prostate hyperplasia using the Rezum® water vapor therapy system: Results at one year. Prog Urol. 2020.	Before and after study **Objective** To report the results of Rezum water vapor therapy on BPH-LUTS and sexual function at one year of follow-up. **Setting**: 2 sites, France **Inclusion criteria** - Rezum® therapy was offered to patients with moderate to severe BPH-related LUTS which was clinically resistant to optimal medical treatment (ineffective, poorly tolerated or refused by the patient) who did not wish to undergo classical surgery. - There were no restrictions regarding prostate volume or conformation in these patients. - initial evaluation consisted of IPSS questionnaire, clinical examination, PSA-test, diagnostic cystoscopy (if required), a urinary tract ultrasound with a prostate volume evaluation, uroflowmetry and post-void residual	**II-3**	62 participants **Baseline characteristics** Mean age : 64.3 ± 11.9 Mean prostate volume: 54.3 ± 28.4 Mean PSA (ng/mL):2.9 ± 2.7 Mean Qmax (mL/s):11.0±3.4 Mean PVR (mL): 78.9 ± 88.9 Mean IPSS score:19.9 ± 6.3 Mean MSHQ-ejd: 8.6 ± 4.9 Mean MSHQ Bother: 2.0 ± 1.7 Mean IIEF5 score:19.4 ± 5.5 **LUTS severity** Moderate 30.6% Severe 56.5% Retention 12.9%	Rezūm therapy -performed at the outpatients department -at the patient's request, the intervention was either done under GA or under hypnosis with slight sedation if required. Hypnosis was performed by an anesthetist or anesthetics nurse trained in medical hypnotherapy. -The patients were catheterized throughout the intervention for duration of 3 days.	No comparator	1, 3, 6 and 12 months	**Functional urinary outcomes** - IPSS decreased significantly by 9.7 points (48.5%), 11.6 points (59.5%), 13.9 points (68.1%) and 12 points (61.5%) respectively at 1, 3, 6 and 12 months compared with the matched reference IPSS ($p < 0.001$). - At one year, the Qmax had increased by an average of 6 mL/s (58.8%, $p < 0.001$).

Outcome measure	Baseline	1 Mos	3 Mos	6 Mos	12 Mos
No. patients	54	54	54	53	41
IPSS					
No. (paired values)	54	50	42	41	41
Mean ± SD baseline	20.0 ± 6.3	20.0 ± 5.8	19.5 ± 5.6	20.4 ± 5.9	19.5 ± 6.1
Mean ± SD follow-up		10.3 ± 5.7	7.9 ± 5.0	6.5 ± 4.2	7.5 ± 4.7
Change ± SD		−9.7 ± 8.4	−11.6 ± 8.7	−13.9 ± 7.9	−12 ± 8.7
% Change		−48.5%	−59.5%	−68.1%	−61.5%
P-value		*< 0.001*	*< 0.001*	*< 0.001*	*< 0.001*
QOL Ipss					
No. (paired values)	54	50	42	41	41
Mean ± SD baseline	4.5 ± 1.0	4.6 ± 0.9	4.5 ± 0.9	4.6 ± 0.9	4.4 ± 1
Mean ± SD follow-up		2.1 ± 1.6	1.5 ± 1.6	1.1 ± 1.4	1.2 ± 1.6
Change ± SD		−2.5 ± 1.7	−3.0 ± 1.8	−3.5 ± 1.6	−3.2 ± 1.7
% Change		−54%	−66%	−76%	−72%
P-value		*< 0.001*	*< 0.001*	*< 0.001*	*< 0.001*
Qmax					
No. (paired values)	54	45	40	33	38
Mean ± SD baseline	11.0 ± 3.4	10.9 ± 3.4	10.7 ± 3.4	10.7 ± 3.4	10.2 ± 3.7
Mean ± SD follow-up		13.2 ± 5.1	14.5 ± 4.8	16.4 ± 5.1	16.2 ± 5.3
Change ± SD		2.4 ± 4.9	3.7 ± 5.4	5.7 ± 5.3	6 ± 4.8
% Change		+23.8%	+31.8%	+53.2%	+58.8%
P-value		*0.006*	*< 0.001*	*< 0.001*	*< 0.001*
RPM					
No. (paired values)	54	45	36	34	32
Mean ± SD baseline	78.9 ± 90	78.8 ± 95.7	75.8 ± 92.2	74.6 ± 93.4	73.3 ± 100
Mean ± SD follow-up		24.2 ± 23.7	25.0 ± 35.5	24.8 ± 25.6	16.9 ± 22.5
Change ± SD		54.6 ± 92.5	−50.8 ± 82.2	−49.8 ± 76.4	−56.4 ± 89.8
% Change		−69%	−67%	−67%	−76%
P-value		*0.002*	*< 0.001*	*0.002*	*0.002*

Sexual function
-The rates of sexually active patients were identical preoperatively (90.7%; 49/54) and at one year.
-The IIEF-5 score (19.4±5.5) was not modified postoperatively and remained stable throughout

volume (PVR) measurement.

Outcome measures
IPSS, IPSS-QoL, Qmax, PVR, IIEF-5, MSHQ-EjD function, MSHQ-EjD bother

the duration of follow-up.
-At 1 year, the MSHQ score had increased by an average of 2 points (p = 0.056).
-Out of 37 patients who were sexually active at one year, 4 patients (10.8%) reported a decrease in ejaculatory volume and 4 patients (10.8%) reported anejaculation.
Adverse events
- No serious adverse events occurred (> Clavien II).
- 22.5% reported no side effects at the one-month follow-up consultation
- Between 3 months and 6 months, two patients spontaneously evacuated a ''bladder stone'' after a serious episode of dysuria. These ''bladder stones'' resulted from calcification of necrotic debris in the bladder.

Adjudicated adverse event	No. events	No. Subjects (%)		Clavien–Dindo classification					
				Grade I	Grade II	Grade IIIa	Grade IIIb	Grade IV	Grade V
Overactive bladder	14	14	22%	6	8	0	0	0	0
Gross hematuria	11	11	17.7%	11	0	0	0	0	0
Painful urination	8	8	12.9%	8	0	0	0	0	0
Urinary tract infection	7	7	11.2%	0	7	0	0	0	0
Urinary retention	7	6	9.6%	7	0	0	0	0	0
Severe dysuria	5	5	8%	3	2	0	0	0	0
Hemospermia	2	2	3.2%	2	0	0	0	0	0
Hemorrhoids crisis	2	2	3.2%	2	0	0	0	0	0
Bladder stone	2	2	3.2%	0	2	0	0	0	0
Clotting hematuria	1	1	1.6%	0	1	0	0	0	0
Painful ejaculation	1	1	1.6%	1	0	0	0	0	0
Pelvic pain	1	1	1.6%	1	0	0	0	0	0
Urinary urgency incontinence	1	1	1.6%	0	1	0	0	0	0
Chronic pelvic pain syndrome	1	1	1.6%	0	1	0	0	0	0
Total	63			41	22	0	0	0	0

Retreatment rate
-surgical retreatment rate of 2.1% at 1 year

Perioperative data
-80.7% general anaesthesia; 19.3% hypnosis (2 patients had hypnosis alone, 7 had slight sedation and/or supplementary antalgic and 3 changed over to general anesthesia for comfort reasons)

							- median duration of treatment was 6 minutes (3—19) with a median number of 5 punctures (2—11) per treatment

Evidence Table : Effectiveness and safety
Question : How safe, effective and cost-saving is the Rezūm therapy for management of LUTS secondary to BPH?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
13. Haroon UM, Khan JS, McNicholas D et al. 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. Ir J Med Sci. 2021.	Before and after study + cost analysis study **Setting:** single centre, Ireland **Objectives:** 1. To evaluate the introduction of this thermal therapy to an Irish teaching hospital for the treatment of LUTs related to BPH. 2. To assess the cost of this new technology per patient to the healthcare institution and compare it to the standard of care, TURP **Inclusion criteria** Men >50 years of age with moderate to severe symptomatic BPH, an IPSS score of > 12, a minimum prostate volume of 30 cc, maximum urinary flow rate (Q-max) < 15 mL/s and a post-void residual (PVR) bladder volume < 500mls. IPSS > 12, Q-max < 12 mL/s and PVR > 50	**II-3**	10 participants Mean age, years :70 ± 9.3 Mean prostate volume: 72 ± 35mls Mean PSA: 4.73 ± 4 ng/mL. Mean baseline IPSS:20.8± 4 Mean IPSS-QOL: 4.4 ± 0.7 Mean Qmax: 9.38 ± 2.42 PVR volume :197 ± 150 mL. <u>LUTS severity</u> Moderate 30% Severe 70%	Rezūm therapy All patients were given general anaesthesia	Effectiveness study- no comparator Cost analysis - TURP	3 months	**Procedure data** -Mean number of treatments to the prostate was 5.2 ± 1.7 with 70% receiving treatment to their median lobe. - Mean duration of post-operative catheterisation following the procedure was 7±3 days. -Mean length of hospital stay was 1.1 days. 80% patients were discharged on the day of surgery. patients stayed overnight for precautionary reasons; 1 because he was 85 years old with poor social circumstances and 1 because a cystolitholapaxy was also performed in the same sitting. **Effectiveness outcomes** -LUTS improved significantly with a 74.5% improvement (15.5 ± 2.5 point reduction) in IPSS from baseline (p < 0.01) and 86% improvement (3.8 point reduction) in IPSS-QOL scores. -Peak flow rate (Q-max) significantly improved by 44%, from a pre-procedure score of 9.26 ± 2.5 to 13.34 ± 2.3 mL/s 3 months post-procedure (p = 0.03). PVR bladder volumes saw a significant (i.e. 74%) reduction from a baseline PVR of 197 ± 150 to 51 ± 22 mL 3 months post-operatively.

$N=10$	Baseline Mean ± SD	3 months Mean ± SD	Change Mean ± SD	%Change	p value
IPSS	20.8 ± 4	5.3 ± 1.49	− 15.5 ± 2.5	74.52%	<0.01*
IPSS-QOL	4.4 ± 0.7	0.6 ± 0.7	3.8	86.36%	<0.01*
Q-max (mL/s)	9.26 ± 2.5	13.34 ± 2.33	4.08 ± 0.19	44.06%	0.03*
PVR (mL)	197 ± 150	51 ± 22	− 146 ± 128	74.11%	<0.01**

Exclusion criteria
Prostate cancer, any active urinary tract infection (UTI) and an indwelling urinary catheter.

Outcome measures
Symptom relief (IPSS) and IPSS quality of life (IPSS-QOL) and uroflowmetry

Cost inputs
-Data obtained from the hospital finance and procurement department -theatre times, equipment/consumables, staff and hospital stay

Breakdown of cost

Consumables	Rezum	TURP
Theatre time	0.5 h	1 h
Theatre cost	€750	1500€
Consultant cost	€47.63	€95.26
Anaesthetic nurse	€13.37	€26.74
Scrub nurse	€13.37	€26.74
Procedure equipment	€1348	€200
Average length of stay (days)	1.1	2.75
Cost of hospital stay	€1527 per day	€1527 per day
Cost of outpatient trial without catheter	€80.00	0

Cost analysis
-Mean total cost of hospital admission for 10 Rezum procedures was €39,623, which was significantly lower than the mean total cost of hospital admission for 10 TURP procedures, €62,442 ($p < 0.01$)
-Intraoperative theatre costs are higher for Rezum when compared to TURP, €2588.27 versus €2054.27.
-The length and cost of stay are significantly lower for Rezum as the average length of stay for Rezum patients was 1.1 days compared to 2.75 days for TURP patients.
-The overall cost per patient for the Rezum procedure and TURP were calculated at €4267.97 and €6253.52, respectively, resulting in a significant cost saving of €1986.52 per patient for Rezūm.

Cost analysis of 10 patients treated with Rezūm and 10 patients treated with TURP in the same period

Cost	Rezum	TURP	*p* value
Total theatre cost	€2588.27	€2054.27	<0.01
Average length of stay	1.1 days	2.75 days	<0.01
Average cost of stay	€1679.70	€4199.25	<0.01
Average cost procedure	€4267.97	€6,253.52	<0.01
Treatment cost 10 pro-spective procedures	€39,623.00	€62,442.00	<0.01

- Overall, for the 10 Rezum cases, there was a total saving of €22,819 to the institution when compared to ten TURP cases and this corresponded into 5 theatre hours and 19 bed days spared.

- If treated purely as day-case and be discharged from the day-ward, further savings further of €623

							saving per Rezum patient compared to TURP [the cost of a discharge for urology day-case was calculated at €904 per day-case compared to €1527 per-day for inpatient admission]. This combination of shorter procedural time and length of stay will allow higher throughput in the department with higher patient turnover and reduced overall cost.

Evidence Table : Cost/Cost-effectiveness
Question : How cost-effective is the Rezūm therapy for management of LUTS secondary to BPH?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Interventions	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
14. Ulchaker JC, Martinson MS. Cost-effectiveness analysis of six therapies for the treatment of lower urinary tract symptoms due to benign prostatic hyperplasia. Clinicoecon Outcomes Res. 2018;10:29-43	Economic evaluation study **Objectives** -To conduct a CEA from payers' perspectives of 6 treatments for lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH) -To examine positioning of these modalities in the marketplace for the best use of health care funds and quality-of-life benefits for patients. **Methods** – using a Markov model – 2 years time horizon with 6 months cycle length – from perspective of the health care payer – Data source : from literature (40 selected articles) – Discount rate : 3%	-	**Clinical inputs** IPSS scores, adverse events, re-treatment rates **Health state utilities** Retreatment and return of the symptoms rates, probabilities of the occurrence of early and late adverse events **Cost inputs** – derived from 2016 Medicare national average fee schedules for the BPH therapies including drugs, diagnostics, and procedures, and treatments for the adverse events.	The six therapies included: 1.Therapy with combination prescription drugs ("ComboRx"), an inhibitor of 5α-reductase (e.g., dutasteride or finasteride), and an α-selective adrenergic receptor blocker (e.g., tamsulosin or doxazosin) 2.The MITs of the following: – The Rezūm therapy – The Prostiva® RF Therapy System (an RF thermal therapy procedure) – The UroLift® System (prostatic urethral lift, permanent implants to retract enlarged prostate tissue) 3. The invasive therapies of the following: – Greenlight laser photovaporization of the prostate (PVP) – Transurethral resection of the prostate (TURP)	2 years	– ComboRx was least effective and provided one-third of the symptom relief achieved with MITs. – UroLift was similar in effectiveness to Prostiva and Rezūm but costs more than twice as much. – The cheaper MITs were ~$900 more expensive than the cost of ComboRx generic drugs over 2 years. – TURP and PVP provided slightly greater relief of LUTS than MITs at approximately twice the cost over 2 years; typically, they are reserved for treatment of more severe LUTS. **Sensitivity analysis** – Comparison was made between therapies on the production possibility frontier: Rezūm versus generic ComboRx and TURP versus Rezūm. – The probabilistic sensitivity analysis indicates that 95% of the time, the cost per additional IPSS point reduction is less than $150 over 2 years when Rezūm is used instead of ComboRx – For 95% of the time, the cost per point reduction is less than $250 over 2 years when TURP is used instead of Rezūm **Conclusion** Since Rezūm is much less expensive, it might be a preferred choice in a health care system seeking to contain costs. The model estimates that on average Rezūm ranks favourably among the MITs.

Evidence Table : Cost/Cost-effectiveness
Question : How cost-effective is the Rezūm therapy for management of LUTS secondary to BPH?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
15. Chughtai B, Rojanasarot S, Neeser K et al. Cost-Effectiveness and Budget Impact of Emerging Minimally Invasive Surgical Treatments for Benign Prostatic Hyperplasia. J Health Econ Outcomes Res. 2021;8(1):42-50.	Economic evaluation study **Objective** - To estimate the cost-effectiveness and budget impact of Prostatic urethral lift (PUL) compared to Rezūm therapy for men with moderate-to-severe BPH from a US Medicare perspective. **Methods** 1.CEA -US Medicare perspective -4 years time horizon with 3-month cycle length was employed in the first year, followed by a 1-year cycle length for years 2 through 4. -Markov modelling -Source of data: safety and efficacy data from the LIFT and Rezum II RCTs -Willingness-to-pay threshold of US$50 000 per quality-adjusted life-year (QALY) gained, 2.BIA -Budget Impact Model (BIM) was developed to compare average per-patient costs of	-	**Population of interest** Cohort of males with a mean age of 63 and an average IPSS of 22 **Clinical inputs** IPSS, LUTS-related AEs, and retreatment rates **Health state utilities** Post-procedure catheterization, LUTS-related AEs, and retreatments **Cost inputs** -Procedural costs, costs associated with AEs, retreatment costs, and follow-up care costs	Rezūm therapy	UroLift	1 year	**1. CEA** - At 1 year, UroLift was associated with lower QALYs (0.917 vs 0.928) and higher total costs (US$6449 vs US$1813) compared to Rezūm therapy -At 4 years, year 4, UroLift resulted in lower QALYs (3.490 vs 3.548) and greater total costs (US$7393 vs US$2233) compared with Rezūm therapy. - With willingness-to-pay threshold of US$50,000/QALY, Rezūm therapy was a more effective and less costly treatment strategy than UroLift for treatment of BPH from years 1 to 4. - The PSA simulations demonstrated that compared with Urolift, Rezūm therapy led to a lower average total cost of US$4978 (SD, 878) and a greater average QALY of 0.060 (SD, 0.031). IPSS change from baseline for UroLift and Rezūm therapy, and the initial treatment cost of UroLift, had the most considerable impact on model results when individually varying each parameter by ±10%. Rezūm therapy was less costly than UroLift 100% of the time and associated with higher QALYs 99% of the time. **2.BIM** -UroLift procedural costs were substantially higher than those of Rezūm therapy (US$5617 versus US$1689). -UroLift was associated with higher total Medicare costs per patient (US$7445 vs US$2257) than Rezūm therapy at 4 years. - 70% total cost difference of UroLift and Rezūm therapy was predominantly driven by higher UroLift procedural (US$5617 vs US$1689) and retreatment (US$976 vs US$257) costs.

	PUL and WVTT using the same model patient flow and clinical and cost inputs as in the CEA.						**Conclusion** Rezūm therapy was the dominant (more effective and less costly) treatment strategy compared to UroLift for the minimally invasive treatment of moderate-to-severe LUTS associated with BPH. Rezūm therapy was a cost-saving treatment option to Medicare relative to UroLift, and the cost difference was predominantly driven by the lower procedural and retreatment costs of Rezūm therapy.

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