BJU Int 2022; **130:** 142–156 doi:10.1111/bju.15653

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Review

Minimally invasive treatments for benign prostatic hyperplasia: a Cochrane network meta-analysis

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Objective

To assess the comparative effectiveness and ranking of minimally invasive treatments (MITs) for lower urinary tract symptoms (LUTS) in men with benign prostatic hyperplasia (BPH).

Materials and Methods

We searched multiple databases up to 24 February 2021. We included randomized controlled trials assessing the following treatments: convective radiofrequency water vapour thermal therapy (WVTT; or Rezūm); prostatic arterial embolization (PAE); prostatic urethral lift (PUL; or Urolift); temporary implantable nitinol device (TIND); and transurethral microwave thermotherapy (TUMT) compared to transurethral resection of the prostate (TURP) or sham surgery. We performed a frequentist network meta-analysis.

Results

We included 27 trials involving 3017 men. The overall certainty of the evidence of most outcomes according to GRADE was low to very low. Compared to TURP, we found that PUL and PAE may result in little to no difference in urological symptoms, while WVTT, TUMT and TIND may result in worse urological symptoms. MITs may result in little to no difference in quality of life, compared to TURP. MITs may result in a large reduction in major adverse events compared to TURP. We were uncertain about the effects of PAE and PUL on retreatment compared to TURP, however, TUMT may result in higher retreatment rates. We were very uncertain of the effects of MITs on erectile function and ejaculatory function. Among MITs, PUL and PAE had the highest likelihood of being the most efficacious for urinary symptoms and quality of life, TUMT for major adverse events, WVTT and TIND for erectile function and PUL for ejaculatory function. Excluding WVTT and TIND, for which there were only studies with short-term (3-month) follow-up, PUL had the highest likelihood of being the most efficacious for retreatment.

Conclusions

Minimally invasive treatments may result in similar or worse effects concerning urinary symptoms and quality of life compared to TURP at short-term follow-up.

Keywords

benign prostatic hyperplasia, lower urinary tract symptoms, minimally invasive treatments, network meta-analysis, transurethral microwave thermotherapy, prostatic urethral lift, temporary implantable nitinol device, prostatic arterial embolization, #Urology, #UroBPH, #UroUTI

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Introduction

Benign prostatic obstruction is a form of BOO and may be diagnosed when the cause of outlet obstruction is known to be BPH [1]. BPH may or may not cause LUTS, which are characterized by urination frequency, hesitancy and a weak stream, mainly in men over the age of 40 years, and has clinical relevance when associated with perceived bother [2]. Symptom bother typically correlates with increased number and severity of symptoms, which are related to impairment in quality of life and treatment-seeking [3]. Although we understand that LUTS comprise a functional unit with a multi-factorial aetiology of associated symptoms, we considered the term BPH for this Cochrane Review because of its familiarity among the general public [4]. The degree of bother across all LUTS can be assessed through self-administered questionnaires, namely, the IPSS (also known as the AUA Symptom Index), which includes a quality-of-life domain [5]. According to an international study involving 7588 men, the prevalence of LUTS was 18% during men's 40s, 29% in their 50s, 40% in their 60s, and 56% in their 70s [6].

Initial treatment options for BPH include conservative management (watchful waiting and lifestyle modification) and the use of medications (alpha-blockers, 5-alpha reductase inhibitors, and, recently, phosphodiesterase inhibitors) [4]. Surgical options are considered when patients have been refractory to conservative and medical treatment or if BPH causes subsequent complications, such as acute urinary retention, recurrent UTI, bladder stones, haematuria, or renal insufficiency [4]. Clinical guidelines continue to recommend monopolar or bipolar TURP as a ('gold') reference standard treatment to provide subjective symptom relief while attaining objective improvement in urinary flow [4,7], but this procedure is associated with some morbidity and long-term complications, including haematuria that may require a blood transfusion, urethral stricture, UTI and incontinence, and it usually requires at least overnight hospitalization. In addition, men may experience ejaculatory (65%) and erectile dysfunction (10%) related to TURP [8]. Furthermore, BPH is a common disease among elderly men, who have increased preoperative risk for complications of general anaesthesia and surgery in general [2]. Recently, several other minimally invasive treatments (MITs) that can be performed in an office setting and do not require general anaesthesia have been developed as alternatives to TURP to provide therapeutic options involving lower morbidity [4]. However, given the relatively high rate of reoperation or continued use of medical therapy after surgical treatment (or both), concern has been raised about the durability of newly launched MITs [9].

Minimally invasive treatments that can be performed in an office setting and do not require general anaesthesia include: a) convective radiofrequency water vapour thermal therapy (WVTT; or Rezūm), which uses thermal energy in the form of water vapour to ablate prostatic tissue [10]; b) prostatic arterial embolization (PAE), which uses super-selective microcatheterization with microspheres to promote tissue necrosis [11]; c) prostatic urethral lift (PUL; or Urolift), which consists of separating and distracting enlarged prostatic tissue by a series of implants to hold excess prostatic tissue out of the way, thereby opening the narrowed urethra without cutting or removing enlarged prostatic tissue [12]; d) temporary implantable nitinol device (TIND), which involves 'reshaping' the prostatic urethra and bladder neck with an implantable device, thereby reducing urinary flow obstruction [13]; and e) transurethral microwave thermotherapy (TUMT), which uses heat into the prostate via electromagnetic radiation of microwaves, inducing coagulation necrosis, reducing prostatic volume [14].

This review aims to assess the comparative effectiveness of MITs for LUTS in men with BPH and obtain an estimate of relative ranking. This is an abridged report of the full Cochrane review [15].

Materials and Methods

Inclusion Criteria

We followed standard Cochrane methods based on a published protocol [16]. We included parallel-group randomized controlled trials (RCTs) including men aged > 40 years with a prostate volume of 20 mL or greater (as assessed by DRE, ultrasonography or cross-sectional imaging) with LUTS (determined by an IPSS of ≥8), and a maximum urinary flow rate (Q_{max}) less than 15 mL/s (as measured by non-invasive uroflowmetry, invasive pressure flow studies, or both) [4]. We excluded trials of men with other conditions that affect urinary symptoms. We included the following MITs, defined as those that do not require general anaesthesia, compared to TURP or sham: WVTT, PAE, PUL, TIND and TUMT. We would also have included head-to-head comparisons between MITs, but none were found. We predefined the structure of the network and its nodes in our protocol [16]. Participants in the network could, in principle, be randomized to any of the methods being compared, and we verified this by comparing characteristics of study design, participants, interventions, and comparisons while considering potential sources of clinical heterogeneity and effect modification (see subgroup analysis and investigation of heterogeneity) [17].

Our main outcomes included urinary symptoms, quality of life, major adverse events, retreatment, erectile function and ejaculatory function. We considered clinically important differences for all outcomes as the basis for rating the certainty of the evidence for imprecision in a 'summary of

findings' table [18]. We considered outcomes measured up to 12 months after randomization as short-term and those measured after 12 months as long-term, except for major adverse events (merging short and long-term data).

Search Methods

We performed a comprehensive search with no restrictions on the language of publication or publication status. We retrieved relevant studies from existing Cochrane Reviews for each treatment [19–22]. We updated searches for each of the individual Cochrane Reviews assessing each MIT. We performed a comprehensive search for TIND from the inception of each of the following databases until 24 February 2021: Cochrane Library via Wiley; MEDLINE via Ovid; Embase via Elsevier; Scopus; Web of Science; Latin American and the Caribbean Health Sciences Literature (LILACS) via Bireme; ClinicalTrials.gov at the US National Institutes of Health (www.clinicaltrials.gov/); and the WHO International Clinical Trials Registry Platform search portal (https://trialsearch.who.int/). We searched the reference lists of included studies, contacted experts, searched the grey literature and screened the abstract proceedings of relevant meetings.

Selection of Studies

We used Covidence software to identify and remove potential duplicate records [23]. Two review authors (J.V.A.F., L.G.) scanned abstracts, titles, or both to determine which studies should be assessed further using the same software, investigating all potentially relevant records as full text, and classified the studies as included studies, excluded studies, studies awaiting classification, or ongoing studies according to the Cochrane Handbook criteria [24]. We resolved any discrepancies through consensus or recourse to a third review author (P.D.). We presented a Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram showing the process of study selection [25].

Data Extraction and Risk-of-Bias Assessment

Because we retrieved relevant studies from existing Cochrane Reviews for each treatment for which study characteristics and outcome data were collected and risk-of-bias assessments were performed by members of our review team [19–22], the following sections apply only to new studies identified by our search methods. For studies that fulfilled the inclusion criteria, two review authors (two of J.V.A.F., L.G. and J.H.J.) independently abstracted the characteristics of the participants, the interventions, comparisons and outcomes, funding sources and conflict of interests. We resolved any disagreements by discussion or, if required, by consultation with a third review author (P.D.). In addition, we contacted the authors of included studies to obtain key missing data as needed. Two review authors (J.V.A.F. and L.G.) independently assessed the risk of bias of each included study using the Cochrane tool for RCTs [26]. We resolved disagreements by consensus or by consultation with a third review author (P.D.).

Statistical Analysis and Certainty of the Evidence

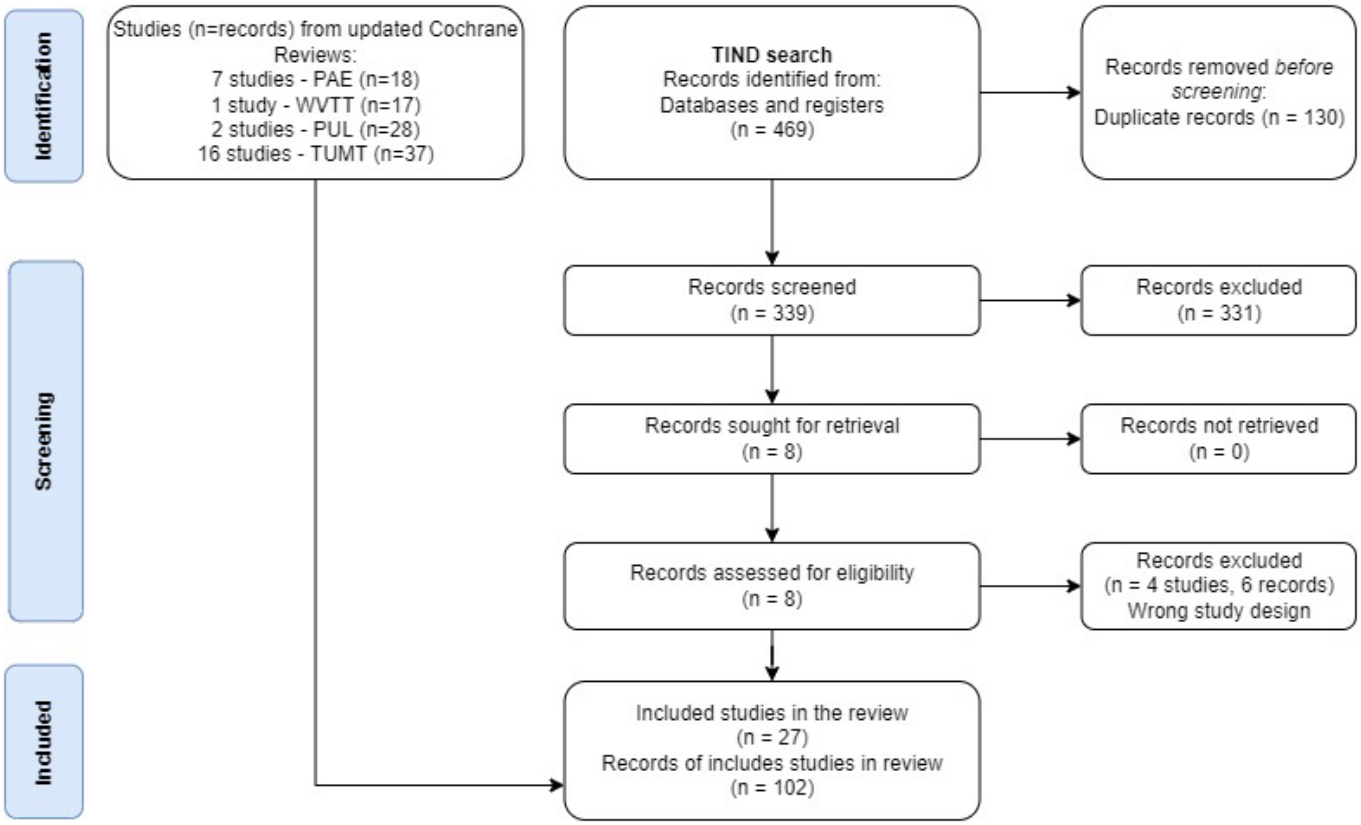
We expressed dichotomous data as risk ratios (RRs) with 95% CIs to enhance the interpretability of results. We expressed continuous data as mean differences (MDs) with 95% CIs. Before conducting a network meta-analysis, we assessed the transitivity assumption by visually inspecting the characteristics of the potential effect modifiers of the included studies across intervention comparisons [27]. We evaluated the presence of inconsistency both locally by loop-specific method and globally by the design-by-treatment interaction model [28,29]. We used comparison-adjusted funnel plots to assess small-study effects indicative of publication bias [30]. We fitted a random-effects network meta-analysis model because we anticipated methodological and clinical heterogeneity across studies. We assumed a common within-network heterogeneity estimate across comparisons, and we estimated this using the restricted maximum likelihood method [31]. We conducted a network meta-analysis using the network suite of commands in Stata (StataCorp. 2019) [29,32,33]. We used the surface under the cumulative ranking curve to rank the effectiveness and safety of MITs [34]. When sufficient studies were available, we intended to perform subgroup analysis by age and severity of symptoms. We also planned to perform sensitivity analyses limited to the primary outcomes to explore the influence of risk of bias by excluding studies at 'high risk' or 'unclear risk'. We used 'summary of findings' tables to summarize key results of the review, using the Confidence in Network Meta-analysis (CINeMA) framework and software [35,36]. We presented an adapted single 'Summary of findings' table for all outcomes, using a modified approach based on the existent guidance [37].

Results

Search Results

We retrieved 26 studies from the previous Cochrane reviews. For the TIND search, we identified 469 records from electronic databases. After removing duplicates, we screened the titles and abstracts of the remaining 339 records, 331 of which we excluded. We assessed eight full-text articles, and we excluded six records for various reasons. Finally, we included one study (two reports) in this review for this intervention. The flow of literature through the assessment process is shown in a PRISMA flowchart (Fig. 1).

Fig. 1 Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram. PAE, prostatic arterial embolization; PUL, prostatic urethral lift; TIND, temporary implantable nitinol device; TUMT, transurethral microwave thermotherapy; WVTT, water vapour thermal therapy.



Characteristics of the Studies Included

We included 27 trials with 3017 randomized participants. Details of the included studies are presented in Table 1. Most studies included men aged > 45–50 years with moderate LUTS refractory to medical treatment, and with a Q_{max} <12/15 mL/s, a voided volume ≥ 125 mL and a prostate volume between 30/100 g and 60/100 g. Participants were usually screened for prostate cancer and infection, among other comorbidities, before inclusion. We included trials with the following interventions and comparisons: WVTT vs sham treatment [38], PAE vs sham treatment [39], PAE vs TURP [40–45], and PUL vs sham treatment [46], PUL vs TURP [47], TIND vs sham treatment [48], TUMT vs sham treatment [49–58], and TUMT vs TURP [59–64]. Half of the studies did not state their funding sources, nine studies were funded by the manufacturers or sponsors of the procedure [38,39,43,46–48,55,57,64], and four were funded by public institutions or hospitals [40,49,56,63]. All studies were considered to have a high or unclear risk of bias, mainly due to lack of blinding in most comparisons, missing outcome data and poor reporting of the characteristics of the included studies. The details for the risk of bias and the characteristics of the excluded and ongoing studies can be found in the full version of the review [15].

Network Meta-Analysis: Minimally Invasive Treatments vs TURP

Considering that most trials assessed the effect of TUMT and PAE, the networks were not densely connected, and in some cases, they were star-shaped with no closed loops. The following analyses present data from networks with no concerns regarding transitivity or global consistency (except in those networks in which it was not possible to assess it due to the lack of closed loops). Table 2 shows a summary of the main findings and Fig. 2 shows a representation of the networks and their corresponding forest plot for each outcome.

Urological symptoms scores

Based on 19 studies with 1847 participants, PUL and PAE may result in little to no difference in urological symptom scores compared to TURP at short-term follow-up

Table 1 Characteristics of the included studies.

Study, year	Trial period	Country	Description of participants	Intervention and comparator	Duration of follow-up	Age, years*	IPSS*	Prostate volume, mL*
Convective radiofrequency WVTT								
McVary et al., 2016 [18]	2013-2014	USA	Men aged ≥ 50 years, symptomatic BPH with IPSS ≥ 13, Q_{max} 5–15 mL/s voided volume ≥ 125 mL, prostate volume 30–80 g	WVTT	3 months	63 ± 7.1	22 ± 4.8	45.8 ± 13.0
				Sham		62.9 ± 7.0	21.9 ± 4.7	44.5 ± 13.3
PAE								
Abt et al., 2018 [40]	2014-2017	Switzerland	Men aged ≥ 40 years, refractory symptoms, prostate 25–80 mL, with IPSS ≥ 8, IPSS-QoL ≥ 3, with Q_{max} < 12 mL/s or urinary retention	PAE	24 months	65.7 ± 9.3	19.38 ± 6.37	52.8 ± 32.0
				TURP		66.1 ± 9.8	17.59 ± 6.17	56.5 ± 31.1
Carnevale et al., 2016 [41]	2010-2012	Brazil	Men aged > 45 years, IPSS > 19, refractory symptoms > 6 months, prostate 30–90 mL, BOO (urodynamic examination)	PAE	12 months	63.5 ± 8.7	25.3 ± 3.6	63.0 ± 17.8
				TURP		66.4 ± 5.6	27.6 ± 3.2	56.6 ± 21.5
Gao et al., 2014 [42]	2007-2012	China	Men with IPSS > 7 after failed medical therapy, prostate volume 20–100 mL, Q_{max} < 15 mL/s	PAE	24 months	67.7 ± 8.7	22.8 ± 5.9	64.7 ± 19.7
				TURP		66.4 ± 7.8	23.1 ± 5.8	63.5 ± 18.6
Insausti et al., 2020 [43]	2014-2017	Spain	Men aged > 60 years, LUTS refractory to medical treatment >6 months, IPSS ≥ 8, IPSS-QoL ≥ 3, Q_{max} ≤ 10 mL/s or urinary retention	PAE	12 months	72.4 ± 6.2	25.8 ± 4.64	60.0 ± 21.6
				TURP		71.8 ± 5.5	26.0 ± 7.29	62.8 ± 23.8
Pisco et al., 2020 [39]	2014-2018	Portugal	Men aged > 45 years; severe LUTS; IPSS ≥ 20 and IPSS-QoL ≥ 3 > 6 months' treatment with alpha-blockers; Q_{max} < 12 mL/s; prostate volume 40 mL	PAE	6 months	64	25.5	63.5
				Sham		64	27.5	66
Radwan et al., 2020 [44]	2016-2018	Egypt	Men with LUTS with an IPSS 8–35, Q_{max} ≤ 10 mL/s; prostate volume < 100 mL	PAE	6 months	63.0 ± 7.2	27.0 ± 5.0	58.7 ± 23.4
				TURP		62.0 ± 9.0	26.5 ± 4.0	60.1 ± 21.5
Zhu et al., 2018 [45]	2016	China	Men with a comprehensive diagnosis of BPH through ultrasound prostate examination, DRE, IPSS, etc.; no absolute contraindication for surgery; no previous history of surgery; not taking 5-alpha reductase inhibitors	PAE	12 months	61.1 ± 4.4	25.63 ± 4.28	81.21 ± 6.34
				TURP		62.4 ± 4.9	26.22 ± 4.35	82.09 ± 6.47

Table 1 (continued)

Study, year	Trial period	Country	Description of participants	Intervention and comparator	Duration of follow-up	Age, years*	IPSS*	Prostate volume, mL*
PUL								
Gratzke et al., 2017 [46]	2012-2013	Europe	Men aged ≥ 50 years with IPSS > 12, Q_{max} ≤ 15 mL/s for 125 mL voided volume, PRV < 350 mL, prostate volume ≤ 60 mL, sexually active, Incontinence Severity Index score ≤ 4	PUL	24 months	63 ± 6.8	22 ± 5.7	38 ± 12
				TURP		65 ± 6.4	23 ± 5.9	41 ± 13
Roehrborn et al., 2013 [47]	2011	19 centres/US, Canada, and Australia	Men aged ≥ 50 years, AUA-SI ≥ 13, Q_{max} ≤ 12 mL/s with a 125 mL voided volume and a 30–80 mL prostate volume	PUL	3 months	67 ± 8.6	22.2 ± 5.48	44.5 ± 12.4
				Sham		65 ± 8.0	24.4 ± 5.75	40.9 ± 10.8
TIND								
Chughtai et al. 2021 [48]	2015-2018	USA/Canada	Men aged ≥ 50 years, symptomatic BPH, IPSS ≥ 10, Q_{max} < 12 mL/s, voided volume > 125 mL, prostate volume 25–75 mL	TIND	3 months	61.5 ± 6.5	22.1 ± 6.8	43.4 ± 15.5
				Sham		60.1 ± 6.3	22.8 ± 6.2	43.8 ± 13.3
TUMT								
Abbou et al., 1995 [49]	N/A	France	Men aged ≥ 50 years with symptoms > 3 months, prostate 30–80 g, Q_{max} < 15 mL/s, PVR < 300 mL	TUMT	12 months	65 ± 8	N/A	45 ± 15
				Sham		66 ± 7	N/A	44 ± 11
Ahmed et al., 1997 [59]	N/A	UK	Men aged ≥ 55 years with AUA score >12 > 1 year, prostate 25–100 mL, Q_{max} < 15 mL/s and a PVR < 300 mL	TUMT	6 months	69.36	18.5	36.6
				TURP		69.45	18.4	46.1
Albala et al., 2002 [50]	N/A	USA	Men aged 50–80 years, AUA-SI index > 13 and a bother score >11, Q_{max} < 12 mL/sec and PVR > 125 mL; prostate 30-100 mL without a significant intravesical middle lobe	TUMT	12 months	65.2 ± 7.3	22.2 ± 5.0	50.5 ± 18.6
				Sham		64.6 ± 7.1	22.7 ± 5.7	47.1 ± 17.9
Bdesha et al., 1994 [51]	N/A	UK	Men with prostatism (WHO score > 14), PVR > 50 mL, Qmax <15 mL/s	TUMT	3 months	63.7	19.2	N/A
				Sham		62.6	18.8	N/A
Blute et al., 1996 [52]	N/A	USA	Men suffering from urinary symptoms (Madsen symptom score >8), PVR 10000 mL, Q_{max} < 10 mL/s, prostate length 30–50 mm	TUMT	12 months	66.9 ± 7.8	19.9 ± 7.2	37.4 ± 14.2
				Sham		66.9 ± 7.1	20.8 ± 6.7	36.1 ± 13.4
Brehmer et al., 1999 [53]	N/A	Sweden	Men experiencing LUTS and with an enlarged prostate	TUMT	12 months	70.4	N/A	N/A
				Sham				

Table 1 (continued)

Study, year	Trial period	Country	Description of participants	Intervention and comparator	Duration of follow-up	Age, years*	IPSS*	Prostate volume, mL*
D'Ancona et al., 1998 [60]	1994-1995	Netherlands	Men ≥ 45 years with Madsen score > 8 months, prostate 2.5-5 cm/30–100 mL, Q_{max} < 15 mL/s PVR < 350 mL	TUMT	24 months	69.6 ± 8.5	16.7 ± 5.6	45 ± 15
				TURP		69.3 ± 5.9	18.3 ± 6.3	43 ± 12
Dahlstrand et al., 1995 [61]	N/A	Sweden	Men ≥ 45 years with Madsen score > 8 months, prostate 3.5–5 cm, Q_{max} < 15 mL/s, PVR > 150 mL	TUMT	24 months	68	N/A	33
				TURP		79	N/A	37
De Wildt et al., 1996 [54]	1991-1992	Netherlands/UK	Men ≥ 45 years with Madsen score > 8 months, Q_{max} < 15 mL/s PVR > 150 mL	TUMT	12 months	63.3 ± 8.1	N/A	48.6 ± 16.6
				Sham		66.9 ± 6.0	N/A	49.0 ± 20.0
Floratos et al., 2001 [62]	1996-1997	Netherlands	Men ≥ 45 years, prostate ≥ 30 cm^3, prostatic urethral length ≥ 25 mm, Madsen symptom score ≥ 8, Q_{max} ≤ 15 mL/s, PVR ≤ 350 mL	TUMT	36 months	68	21	42
				TURP		66	20	48
Larson et al., 1998 [55]	1994-1996	USA	Men aged ≥ 45 years with AUA score > 9, enlarged prostate (3–5 cm TRUS), Q_{max} < 12 mL/s without a significantly enlarged middle lobe	TUMT	12 months	66	20.8	38.1
				Sham		65.9	21.3	44.7
Nawrocki et al., 1997 [56]	N/A	UK	Men with a Madsen symptom score ≥ 8, Q_{max} ≤ 15 mL/s, PVR > 150 mL, detrusor pressure > 70 cm H_2O	TUMT	6 months	70	19	41.2 ± 14.6
				Sham			17.5	46.7 ± 16.8
Norby et al., 2002 [63]	1996-1997	Denmark	Men aged ≥ 50 years, IPSS ≥ 7, Q_{max} ≤ 12 mL/s	TUMT	6 months	66 ± 7	20.5 ± 5.7	43
				TURP/TUIP		68 ± 7	21.3 ± 6.6	44
Roehrborn et al., 1998 [57]	N/A	United States	Men aged ≥ 55 years, AUA-SI ≥ 13, Q_{max} ≤ 12 mL/s, prostate volume 25–100 mL	TUMT	6 months	66.3 ± 6.5	23.6 ± 5.6	48.1 ± 16.2
				Sham		66.0 ± 5.8	23.9 ± 5.6	50.5 ± 18.1
Venn et al., 1995 [58]	N/A	UK	Men with a Madsen symptom score ≥ 8, PVR < 250 mL	TUMT	6 months	70.5	19.2	40.4
				Sham		68	20.1	40.6
Wagrell et al., 2002 [64]	1998-1999	Scandinavia/USA	Men IPSS ≥ 13, Q_{max} ≤ 13 mL/s, prostate volume 30–100 mL	TUMT	5 years	67 ± 8	21.0 ± 5.4	48.9 ± 15.8
				TURP		69 ± 8	20.4 ± 5.9	52.7 ± 17.3

*AUA-SI, AUA Symptom Index; PAE, prostatic arterial embolization; PUL, prostatic urethral lift; PVR, postvoid residual urine volume; Q_{max}, maximum urinary flow rate; TIND, temporary implantable nitinol device; TUMT, transurethral microwave thermotherapy; WVTT, water vapour thermal therapy. *Mean/median, ± SD when available.*

(3−12 months; MD of IPSS [range 0 to 35, higher scores indicate worse symptoms] for PUL: 1.47, 95% CI −4.00 to 6.93; for PAE: 1.55, 95% CI −1.23 to 4.33). WVTT, TUMT and TIND may result in worse urological symptoms scores compared to TURP at short-term follow-up, but the CIs include little to no difference (WVTT: 3.6, 95% CI −4.25 to 11.46; TUMT: 3.98, 95% CI 0.85 to 7.10; TIND: 7.5, 95% CI −0.68 to 15.69). TURP had the highest likelihood of being the most efficacious for this outcome; however, among minimally invasive procedures, PUL and PAE were the highest-ranked interventions. The certainty of the evidence was low because of major concerns about within-study bias, imprecision and inconsistency.

Quality of life

Based on 13 studies with 1469 participants, all interventions (PUL, PAE, WVTT, TUMT, TIND) may result in little to no difference in quality-of-life scores compared to TURP at short-term follow-up (3−12 months; MD of IPSS-Quality-of-Life score [range 0–6, higher scores indicate worse symptoms] for PUL: 0.06, 95% CI −1.17 to 1.30; for PAE: 0.09, 95% CI −0.57 to 0.75; for WVTT: 0.37, 95% CI −1.45 to 2.20; for TUMT: 0.65, 95% CI −0.48 to 1.78; for TIND: 0.87, 95% CI −1.04 to 2.79). TURP had the highest likelihood of being the most efficacious for this outcome; however, among MITs, PUL and PAE were the highest-ranked interventions. The certainty of the evidence was low because of major concerns regarding within-study bias, imprecision and inconsistency.

Major adverse events

Based on 15 studies with 1573 participants, TUMT probably results in a large reduction in major adverse events compared to TURP (RR 0.20, 95% CI 0.09 to 0.43). PUL, WVTT, TIND and PAE may also result in a large reduction in major adverse events, but the CI includes substantial benefits and harms (at 3−36 months, PUL: RR 0.30, 95% CI 0.04 to 2.22; WVTT: RR 0.37, 95% CI 0.01 to 18.62; TIND: 0.52, 95% CI 0.01 to 24.46; PAE: 0.65, 95% CI 0.25 to 1.68). Furthermore, TUMT had the highest likelihood of being the most efficacious for this outcome, while TURP was the lowest-ranked intervention. The certainty of the evidence was low for WVTT, TIND, PUL and PAE because of major concerns regarding within-study bias and severe imprecision. The certainty of the evidence for TUMT was moderate because of major concerns regarding within-study bias.

The most commonly reported major adverse events included haematuria with blood clots requiring evacuation or transfusion and severe infection. Less frequently and with a delayed presentation, some patients developed meatal/urethral stenosis, which usually required additional procedures for resolution (bladder neck incision/urethrotomy).

Retreatment

Based on 10 studies with 799 participants, we were uncertain about the effects of PAE and PUL on retreatment compared to TURP at long-term follow-up (12−60 months; PUL: RR 2.39, 95% CI 0.51 to 11.1; PAE: RR 4.39, 95% CI 1.25 to 15.44). TUMT may result in a higher increase in retreatment rates (RR 9.71, 95% CI 2.35 to 40.13). TURP had the highest likelihood of being the most efficacious for this outcome; however, PUL was the highest-ranked intervention among MITs. The certainty of the evidence was very low for PUL and PAE due to major concerns about the within-study bias, imprecision, inconsistency and incoherence. The certainty of the evidence for TUMT was low due to major concerns about within-study bias and incoherence.

These results do not include WVTT or TIND because of short-term follow-up (these results are displayed separately below, under pairwise comparisons).

Erectile function

Based on six studies with 640 participants (Abt et al. 2018; Carnevale 2016; Chughtai 2020; Gratzke 2017; McVary 2016; Roehrborn 2013), we are very uncertain of the effects of MITs on erectile function (MD of IIEF-5 [range 5 to 25, higher scores indicate better function]: WVTT: 6.49, 95% CI −8.13 to 21.12; TIND: 5.19, 95% CI −9.36 to 19.74; PUL: 3.00, 95% CI −5.45 to 11.44; PAE: −0.03, 95% CI −6.38 to 6.32). WVTT and TIND had the highest likelihood of being the most efficacious for this outcome, while TURP was the lowest-ranked intervention; the certainty of the evidence was very low due to major concerns about the within-study bias, incoherence and severe imprecision.

Studies related to TUMT did not report this outcome as defined in this analysis (these results are displayed separately below in pairwise comparisons).

Ejaculatory function

Based on eight studies with 461 participants, we are uncertain of the effects of PUL, PAE and TUMT on ejaculatory dysfunction compared to TURP (at 3−12 months, PUL: RR 0.05, 95% CI 0.00 to 1.06; PAE: RR 0.35, 95% CI 0.13 to 0.92; TUMT: RR 0.34, 95% CI 0.17 to 0.68). PUL has the highest likelihood of being the most efficacious for this outcome, while TURP was the lowest-ranked intervention. The certainty of the evidence was very low due to major concerns about within-study bias, inconsistency, and incoherence. WVTT was not included in this section because these studies were disconnected from the network (see description below). In addition, the study assessing TIND reported no events of ejaculatory dysfunction.

Table 2 Summary of findings table.

Patient or population: men with moderate to severe LUTS due to BPH Interventions: minimally invasive treatments Comparator (reference): TURP Setting: hospital procedure, outpatient follow-up				
Outcome: urinary symptom scores, measured by: IPSS range 0–35 (lower scores indicate fewer symptoms); follow-up: 3–12 months (most of the data are from 3-month follow-up)				
19 studies 1847 participants	**Anticipated absolute effect (95% CI)***		**Certainty of the evidence**	**Ranking (SUCRA)†**
	With TURP	**With a minimally invasive procedure**		
PUL (UroLift; mixed estimate)	Mean score in the included studies: 6.82 (range 5.1 to 12.6)[a]	1.47 higher (4.00 lower to 6.93 higher)	⊕⊕⊖⊖ Low	2.8 (70.5%)
PAE (mixed estimate)		1.55 higher (1.23 lower to 4.33 higher)	⊕⊕⊖⊖ Low	2.9 (69.2%)
WVTT (Rezūm; indirect estimate)		3.60 higher (4.25 lower to 11.46 higher)	⊕⊕⊖⊖ Low	3.9 (52.4%)
TUMT (mixed estimate)		3.98 higher (0.85 higher to 7.10 higher)	⊕⊕⊖⊖ Low	4.4 (43.0%)
TIND (indirect estimate)		7.50 higher (0.68 lower to 15.69 higher)	⊕⊕⊖⊖ Low	5.5 (21.5%)
Outcome: quality of life, measured by: IPSS-QoL range 0–6 (lower scores indicate a lesser impact on quality of life); follow-up: 3–12 months				
13 studies 1469 participants	**Anticipated absolute effect (95% CI)***		**Certainty of the evidence**	**Ranking (SUCRA)†**
	With TURP	**With MIT**		
PUL (UroLift; mixed estimate)	Mean score in the included studies: 2.09 (range 0.9–3.26)[a]	0.06 higher (1.17 lower to 1.30 higher)	⊕⊕⊖⊖ Low	2.8 (70.3%)
PAE (mixed estimate)		0.09 higher (0.57 lower to 0.75 higher)	⊕⊕⊖⊖ Low	2.9 (68.1%)
WVTT (Rezūm; indirect estimate)		0.37 higher (1.45 lower to 2.20 higher)	⊕⊕⊖⊖ Low	3.6 (56.3%)
TUMT (mixed estimate)		0.65 higher (0.48 lower to 1.78 higher)	⊕⊕⊖⊖ Low	4.5 (42.2%)
TIND (indirect estimate)		0.87 higher (1.04 lower to 2.79 higher)	⊕⊕⊖⊖ Low	5.0 (33.4%)
Outcome: major adverse events, defined as Clavien–Dindo Grade III, IV and V, including hospitalizations and procedures to treat complications related to the initial intervention; follow-up: 3–36 months				
15 studies 1573 participants	**Anticipated absolute effect (95% CI)***		**Relative effect (95% CI)**	**Certainty of the evidence**	**Ranking (SUCRA)†**
	With TURP	**With MIT**			
TUMT (mixed estimate)	Median rate of major adverse events: 130 per 1000[a]	104 fewer per 1000 (118 fewer to 74 fewer)	RR 0.20 (0.09 to 0.43)	⊕⊕⊕⊖ Moderate	2.7 (72.1%)
PUL (UroLift; mixed estimate)		90 fewer per 1000 (125 fewer to 159 more)	RR 0.30 (0.04 to 2.22)	⊕⊕⊖⊖ Low	3.6 (56.9%)
WVTT (Rezūm; indirect estimate)		81 fewer per 1000 (129 fewer to 870 more)	RR 0.37 (0.01 to 18.68)	⊕⊕⊖⊖ Low	4.0 (50.0%)
TIND (indirect estimate)		63 fewer per 1000 (129 fewer to 870 more)	RR 0.52 (0.01 to 24.46)	⊕⊕⊖⊖ Low	4.3 (44.7%)
PAE (mixed estimate)		45 fewer per 1000 (97 to 89 more)	RR 0.65 (0.25 to 1.68)	⊕⊕⊖⊖ Low	5.0 (33.6%)
Outcome: retreatment, defined as number of participants requiring a follow-up procedure for LUTS including another MIT or TURP (this does not include procedures to treat complications; these are included under major adverse events); follow-up: 12–60 months					
10 studies 799 participants	**Anticipated absolute effect (95% CI)***		**Relative effect (95% CI)**	**Certainty of the evidence**	**Ranking (SUCRA)†**
	With TURP	**With MIT**			
PUL (UroLift; mixed estimate)	Median rate of retreatment: 12 per 1000[a]	17 more per 1000 (6 fewer to 121 more)	RR 2.39 (0.51 to 11.10)	⊕⊖⊖⊖ Very low	2.2 (68.8%)
PAE (mixed estimate)		41 more per 1000 (3 more to 173 more)	RR 4.39 (1.25 to 15.44)	⊕⊖⊖⊖ Very low	3.0 (50.8%)
TUMT (mixed estimate)		104 more per 1000 (16 more to 470 more)	RR 9.71 (2.35 to 40.13)	⊕⊕⊕⊖ Low	3.7 (32.1%)

Table 2 (continued)

Outcome: retreatment, defined as number of participants requiring a follow-up procedure for LUTS including another MIT or TURP (this does not include procedures to treat complications; these are included under major adverse events); follow-up: 12–60 months					
10 studies 799 participants	**Anticipated absolute effect (95% CI)***		**Relative effect (95% CI)**	**Certainty of the evidence**	**Ranking (SUCRA)†**
	With TURP	**With MIT**			
WVTT (Rezūm; pairwise)	We are very uncertain about the effects of WVTT on retreatment compared to sham at 3 months follow-up (RR 1.36, 95% CI 0.06 to 32.86, 1 study, 197 participants).			⊕⊖⊖⊖ Very low	Not in NMA
TIND (pairwise)	We are very uncertain about the effects of TIND on retreatment compared to sham at 3-month follow-up (RR 0.67, 95% CI 0.11 to 3.89, 1 study, 185 participants).			⊕⊖⊖⊖ Very low	Not in NMA
Outcome: erectile function, measured by IIEF score (range 5–25; higher scores indicate better function); follow-up 3–12 months					
6 studies 640 participants	**Anticipated absolute effect (95% CI) ***			**Certainty of the evidence**	**Ranking (SUCRA)†**
	With TURP	**With MIT**			
WVTT (Rezūm; indirect estimate)	Mean score in the included studies: 15.16 (range 11.67 to 17.70)[a]	6.49 higher (8.13 lower to 21.12 higher)		⊕⊖⊖⊖ Very low	2.5 (70.7%)
TIND (indirect estimate)		5.19 higher (9.36 lower to 19.74 higher)		⊕⊖⊖⊖ Very low	2.9 (61.7%)
PUL (UroLift; mixed estimate)		3.00 higher (5.45 lower to 11.44 higher)		⊕⊖⊖⊖ Very low	3.5 (49.5%)
PAE (mixed estimate)		0.03 lower (6.38 lower to 6.32 higher)		⊕⊖⊖⊖ Very low	4.4 (31.1%)
TUMT	Not reported				
Outcome: ejaculatory function, defined as men with ejaculatory dysfunction, loss or substantial reduction in ejaculation (as an indication of retrograde ejaculation); follow-up: 3–12 months					
8 studies 461 participants	**Anticipated absolute effect (95% CI)***		**Relative effect (95% CI)**	**Certainty of the evidence**	**Ranking (SUCRA)†**
	With TURP	**With MIT**			
PUL (UroLift; mixed estimate)	Median rate of ejaculatory dysfunction: 550 per 1000	521 fewer per 1000 (549 fewer to 32 more)	RR 0.05 (0.01 to 1.06)	⊕⊖⊖⊖ Very low	1.2 (92.1%)
TUMT (mixed estimate)		364 fewer per 1000 (458 fewer to 173 fewer)	RR 0.34 (0.17 to 0.68)	⊕⊖⊖⊖ Very low	2.3 (55.1%)
PAE (mixed estimate)		356 fewer per 1000 (476 fewer to 42 fewer)	RR 0.35 (0.13 to 0.92)	⊕⊖⊖⊖ Very low	2.5 (51.1%)
WVTT (Rezūm; pairwise)	Based on one study with 131 participants, WVTT may result in little to no difference in events of ejaculatory dysfunction compared to sham at short-term follow-up (RR 4.01, 95% CI 0.22 to 72.78).			⊕⊖⊖⊖ Very low	Not in NMA
TIND (pairwise)	The study assessing TIND compared to sham reported no events of ejaculatory dysfunction.			⊕⊖⊖⊖ Very low	Not in NMA

*GRADE Working Group grades of evidence (or certainty of the evidence); MIT, minimally invasive treatment; NMA, network meta-analysis; PAE, prostatic arterial embolization; PUL, prostatic urethral lift; RR, risk ratio; SUCRA, surface under the cumulative ranking curve; TIND, temporary implantable nitinol device; TUMT, transurethral microwave thermotherapy; WVTT, water vapour thermal therapy. High certainty: we are very confident that the true effect lies close to that of the estimate of the effect. Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the effect estimate. Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect. *Estimates are reported as risk difference and CI. †Rank statistics are defined as the probability that a treatment out of n treatments in a network meta-analysis is the best, the second, the third, and so on until the least effective treatment. SUCRA estimates are in brackets.*

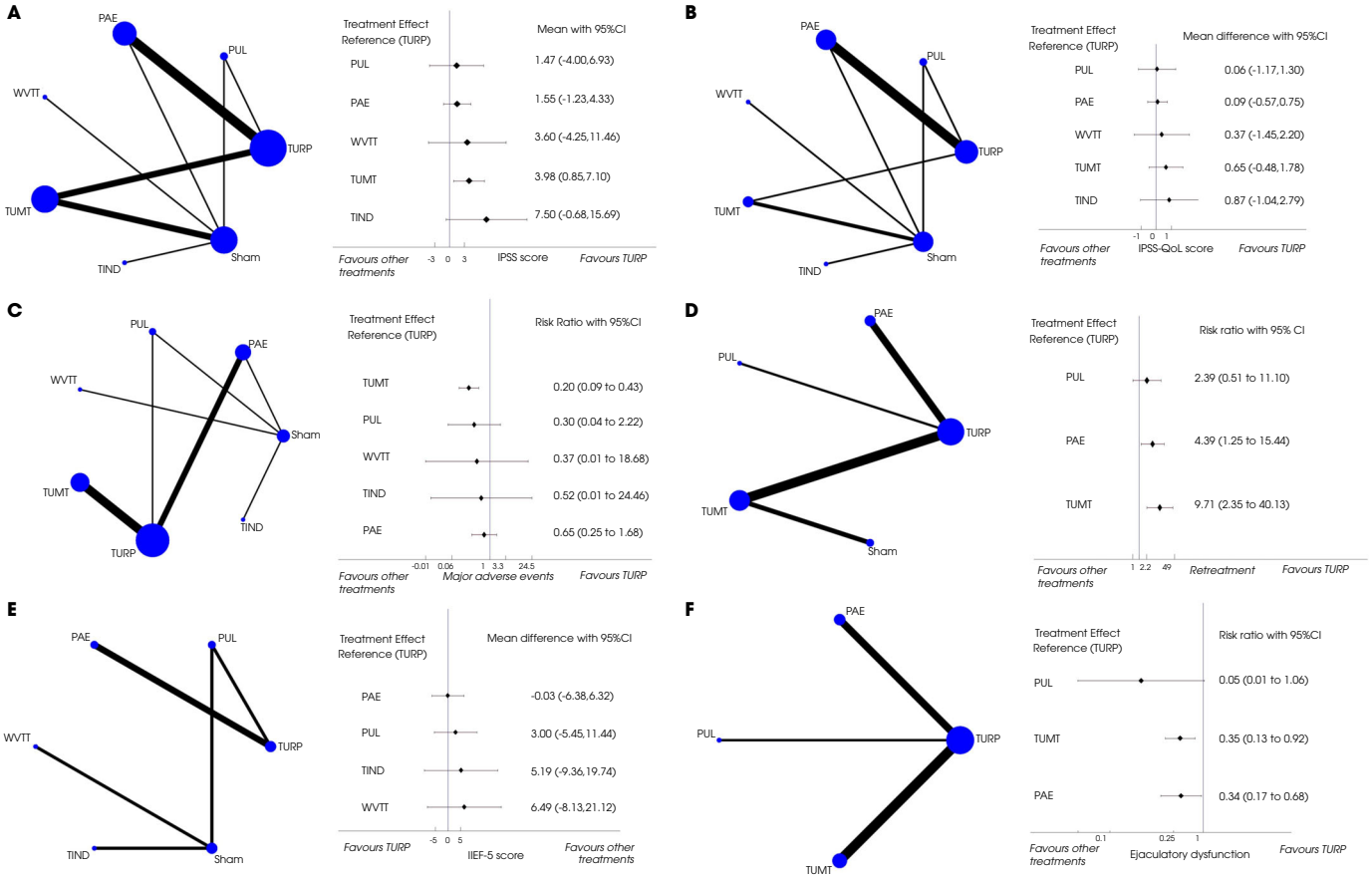


Fig. 2 Network maps and forest plots. IIEF, International Index of Erectile Function; PAE, prostatic arterial embolization; PUL, prostatic urethral lift; TIND, temporary implantable nitinol device; TUMT, transurethral microwave thermotherapy; WVTT, water vapour thermal therapy.

Pairwise Comparisons

We describe here some key information that we were unable to include in our network meta-analysis to preserve the transitivity of each network.

Retreatment: water vapour thermal therapy and temporary implantable nitinol device

Based on one study with 197 participants, we are uncertain about the effects of WVTT on retreatment compared to sham treatment at 3 months follow-up (RR 1.36, 95% CI 0.06 to 32.86) [38]. Based on another study with 185 participants, we are very uncertain about the effects of TIND on retreatment compared to sham treatment at 3-month follow-up (RR 0.67, 95% CI 0.11 to 3.89) [48]. The certainty of the evidence was very low due to concerns about risk of bias and severe imprecision. These results could not be included in the network due to their short-term follow-up.

Erectile function: transurethral microwave thermotherapy

Based on four studies with 278 participants, TUMT may result in little to no difference in erectile function (defined as an event of erectile dysfunction) compared to TURP at short-term follow-up (RR 0.79, 95% CI 0.40 to 1.55; $I^2 = 0\%$). One study found a similar result at long-term follow-up (RR 0.49, 95% CI 0.17 to 1.41) [64]. However, the certainty of the evidence was low due to concerns about risk of bias and imprecision. These results could not be included in the network because they were assessed as binary data and not IIEF scores.

Ejaculatory function: water vapour thermal therapy

Based on one study with 131 participants, WVTT may result in little to no difference in events of ejaculatory dysfunction compared to sham treatment at short-term follow-up (RR 4.01, 95% CI 0.22 to 72.78) [38]. The certainty of the

evidence was low due to concerns about risk of bias and imprecision. These results could not be included in the network because they were disconnected from all nodes.

Subgroup analysis

We found no subgroup differences in urological symptom scores according to age or symptom severity. We found no subgroup differences in quality of life according to age. Most of the prespecified subgroup analyses were not possible to perform due to the scarcity of data.

Discussion

We included 27 trials with 3017 randomized participants, assessing the effects of MITs compared to TURP or sham treatment. TURP is the reference treatment and was found to have the highest likelihood of being the most efficacious for urinary symptoms, quality of life, retreatment, minor adverse events, and acute urinary retention, but the least favourable in terms of major adverse events, erectile function and ejaculatory function. Among MITs, PUL and PAE had the highest likelihood of being the most efficacious for urinary symptoms and quality of life, and TUMT for major adverse events, PUL for retreatment, ejaculatory function and acute urinary retention, WVTT and TIND for erectile function, and PAE for minor adverse events.

The largest limitation of this study relates to issues related to the underlying body of evidence (see below), particularly the lack of head-to-head trials for MITs against TURP. For example, RCTs for WVTT and TIND were limited to comparisons against sham treatment that were unblinded after 3 months and had a short-term follow-up in many cases. The latter issues are underscored by the fact that the AUA guideline panel on the surgical management of LUTS had determined it required a minimum follow-up of longer than 12 months to support its recommendations [65,66]. Since longer-term RCT data are so limited, observational data may provide complementary information. For example, a systematic review of such studies found that the retreatment rate may be higher for PUL than assessed in the present review, at close to 6% per year [67]. Meanwhile, another systematic review has suggested that the long-term effects of WVTT may be sustained with a relatively low retreatment rate [68].

The reporting of adverse events was not uniform across studies, especially of those that differ across procedures, such as 'post-embolization syndrome' in PAE. This was also highlighted in a recent review of observational data in which over a quarter of patients experienced this syndrome, but it was not uniformly characterized [69]. Although the Clavien–Dindo system provides a well-established system to grade the severity of surgical complications, it may be less than ideal to characterize, for example, the adverse event profile for such different MITs as PUL and PAE.

A recent systematic review on men's values and preferences highlighted that men expect a high success rate with low remission and complication rates, which MITs may provide compared to TURP [70]. However, men also value the preservation of their sexual function, for which there are greater uncertainties. Therefore, clinicians must engage in shared decision-making with their patients when discussing the available options [71].

The certainty of the evidence was mostly low to very low owing to risk of bias, imprecision, inconsistency and the inability to assess incoherence in loosely connected networks. There is also the possibility of novelty bias, which refers to the mere appearance that a new treatment is better when it is new [27,72]. We made minor modifications from our protocol regarding the reporting of additional data available in each supporting review and the display of the ranking results both graphically and in the 'Summary of findings' tables. All these changes were duly documented in the full version of the review [15]. We could not include all available trials and interventions in all networks, primarily because of the lack of reporting of the outcomes in the desired format or definition. Finally, we could not perform subgroup and sensibility analyses due to the limited representation of subgroups in trials. Moreover, sensitivity analyses were not possible, considering that most of the studies were at a high or unclear risk of bias.

We identified several systematic reviews focusing on MITs, reporting similar findings concerning the efficacy of TIND, PUL, PAE and WVTT, and highlighting that these are relatively effective treatments, with a lower incidence of adverse events and sexual dysfunction, compared to TURP [73–78]. While some of these findings are similar to those of the present review, we highlight the uncertainty surrounding some of these outcomes, especially those related to sexual function, in which the data are sparse and usually available for only a subset of participants in each study, as was highlighted by one review [79]. Furthermore, many of these reviews included evidence from non-randomized studies and had an overall low quality [80,81]. In some cases, the evidence was synthesized by the authors of the primary studies [73]. Finally, there is a paucity of reviews focusing on TUMT in the last few years as no trials have been reported since the previous version of the Cochrane Review [82].

In conclusion, MITs may result in similar or worse effects concerning urinary symptoms and quality of life, compared to the standard treatment (TURP) at short-term follow-up. They may result in a large reduction of major adverse events, especially in the use of PUL and PAE, which resulted in better rankings for symptom scores. PUL may result in fewer

retreatments than other interventions, especially TUMT, which has the highest retreatment rates at long-term follow-up. We are very uncertain about the effects of these interventions on erectile function; however, these treatments may result in fewer cases of ejaculatory dysfunction. Considering that patients value the effects of these treatments on urinary symptoms, retreatment rates, and adverse events, including sexual function, it becomes necessary to engage in shared decision-making when discussing patients' different treatment options, highlighting the existing uncertainties and eliciting their preferences.

There needs to be better reporting of basic trial methodology and a greater emphasis on patient-reported outcomes, especially those related to sexual function. Many studies broke the blinding period after 3 months and patients crossed to the active treatment group, which prevented us from knowing the long-term effects of these interventions. This is particularly relevant for WVTT and TIND, both of which are supported only by single trials that compared the new therapeutic approach to sham control, with a 3-month time horizon. Sham-controlled trials provide only limited and indirect evidence to inform decision-making, and future research could focus on active comparisons and patient-important outcomes with a follow-up longer than 12 months [65,66,83]. A core outcome set should establish which outcomes should be collected and how and when they should be collected.

Acknowledgements

This project was funded by the National Institute for Health Research (NIHR; Cochrane Incentive Award [NIHR130819]). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care. We are very grateful to Cochrane Urology, especially Managing Editor Robert Lane, as well as Cochrane Urology Korea, for supporting this review. We are also grateful for the constructive feedback from the Cancer Network and the Methods Support Unit. We also thank Gretchen Kuntz for revising and providing feedback on the search strategies, Marco Blanker, Sevann Helo and Murad Mohammad for their peer review input on the protocol, Dominik Abt, Bilal Chughtai and Ahmed Higazy for providing details of the outcomes of their trials so they could be incorporated accurately in our review, and Marc Sapoval, Deepak Agarwal, Cameron Alexander, Harris Foster and Mitchell Humphreys for their peer review input on the review. Juan Víctor Ariel Franco is a PhD candidate in the Programme of Methodology of Biomedical Research and Public Health, Universitat Autònoma de Barcelona (Spain).

Conflict of Interest

Juan V. A. Franco, Jae Hung Jung, Mari Imamura, Jafar Golzarian, Muhammad Imran Omar, Camila Micaela Escobar Liquitay, Areti Angeliki Veroniki, Luis Garegnani and Philip Dahm: none declared. Shamar Young: Boston Scientific (speaker), Galvanize (consultant). Michael Borofsky: Boston Scientific (Consultant for Endourology and Stone Management), Auris Health (Consultant for Robotic Surgery and Endourology), Urotronic (Disease Monitoring and Safety Board).

References

1 **Abrams P**, **Cardozo L**, **Fall M et al**. The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society. *Urology* 2003; 61: 37–49

2 **Dunphy C**, **Laor L**, **Te A**, **Kaplan S**, **Chughtai B**. Relationship between depression and lower urinary tract symptoms secondary to benign prostatic hyperplasia. *Rev Urol* 2015; 17: 51–7

3 **Agarwal A**, **Eryuzlu LN**, **Cartwright R et al**. What is the most bothersome lower urinary tract symptom? Individual- and population-level perspectives for both men and women. *Eur Urol* 2014; 65: 1211–7

4 EAU Guidelines: Management of Non-neurogenic Male LUTS. 2015. Available at: https://uroweb.org/guideline/treatment-of-non-neurogenic-male-luts. Accessed June 13, 2021

5 **Barry MJ**, **Williford WO**, **Chang Y et al**. Benign prostatic hyperplasia specific health status measures in clinical research: how much change in the American urological association symptom index and the benign prostatic hyperplasia impact index is perceptible to patients? *J Urol* 1995; 154: 1770–4

6 **Homma Y**, **Kawabe K**, **Tsukamoto T et al**. Epidemiologic survey of lower urinary tract symptoms in Asia and Australia using the international prostate symptom score. *Int J Urol* 1997; 4: 40–6

7 **Alexander CE**, **Scullion MMF**, **Omar MI et al**. Reprint - Bipolar vs. monopolar transurethral resection of the prostate for lower urinary tract symptoms secondary to benign prostatic obstruction: A Cochrane review. *Can Urol Assoc J* 2020; 14: 423–30

8 **McVary KT**, **Roehrborn CG**, **Avins AL et al**. Update on AUA guideline on the management of benign prostatic hyperplasia. *J Urol* 2011; 185: 1793–803

9 **Strope SA**, **Vetter J**, **Elliott S**, **Andriole GL**, **Olsen MA**. Use of medical therapy and success of laser surgery and transurethral resection of the prostate for benign prostatic hyperplasia. *Urology* 2015; 86: 1115–22

10 **Woo HH**, **Gonzalez RR**. Perspective on the Rezūm® System: a minimally invasive treatment strategy for benign prostatic hyperplasia using convective radiofrequency water vapor thermal therapy. *Med Devices* 2017; 10: 71–80

11 **DeMeritt JS**, **Elmasri FF**, **Esposito MP**, **Rosenberg GS**. Relief of benign prostatic hyperplasia-related bladder outlet obstruction after transarterial polyvinyl alcohol prostate embolization. *J Vasc Interv Radiol* 2000; 11: 767–70

12 **McNicholas TA**. Benign prostatic hyperplasia and new treatment options - a critical appraisal of the UroLift system. *Med Devices* 2016; 9: 115–23

13 **Porpiglia F**, **Fiori C**, **Bertolo R**, **Garrou D**, **Cattaneo G**, **Amparore D**. Temporary implantable nitinol device (TIND): a novel, minimally invasive treatment for relief of lower urinary tract symptoms (LUTS) related to benign prostatic hyperplasia (BPH): feasibility, safety and functional results at 1 year of follow-up. *BJU Int* 2015; 116: 278–87

14 **Rubeinstein JN**, **McVary KT**. Transurethral microwave thermotherapy for benign prostatic hyperplasia. *Int Braz J Urol* 2003; 29: 251–63

15 **Franco JVA**, **Jung JH**, **Imamura M et al**. Minimally invasive treatments for lower urinary tract symptoms in men with benign prostatic hyperplasia: a network meta-analysis. *Cochrane Database Syst Rev* 2021; 7: CD013656

16 **Franco JVA**, **Jung JH**, **Imamura M et al**. Minimally invasive treatments for lower urinary tract symptoms in men with benign prostatic hyperplasia: a network meta-analysis. *Cochrane Libr* 2020; 2020: CD013656

17 **Salanti G**. Indirect and mixed-treatment comparison, network, or multiple-treatments meta-analysis: many names, many benefits, many concerns for the next generation evidence synthesis tool. *Res Synth Methods* 2012; 3: 80–97

18 **Johnston BC**, **Patrick DL**, **Busse JW**, **Schünemann HJ**, **Agarwal A**, **Guyatt GH**. Patient-reported outcomes in meta-analyses–Part 1: assessing risk of bias and combining outcomes. *Health Qual Life Outcomes* 2013; 11: 109

19 **Franco JVA**, **Garegnani L**, **Liquitay CME**, **Borofsky M**, **Dahm P**. Transurethral microwave thermotherapy for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia. *Cochrane Database Syst Rev* 2021; 2021: CD004135

20 **Jung JH**, **Reddy B**, **McCutcheon KA et al**. Prostatic urethral lift for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia. *Cochrane Database Syst Rev* 2019; 5: CD012832

21 **Jung JH**, **McCutcheon KA**, **Borofsky M et al**. Prostatic arterial embolization for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia. *Cochrane Database Syst Rev* 2020; 12: CD012867.

22 **Kang TW**, **Jung JH**, **Hwang EC**, **Borofsky M**, **Kim MH**, **Dahm P**. Convective radiofrequency water vapour thermal therapy for lower urinary tract symptoms in men with benign prostatic hyperplasia. *Cochrane Database Syst Rev* 2020; 3: CD013251

23 **Veritas Health Innovation, Melbourne, Australia**. Covidence systematic review software. Available from: www.covidence.org

24 **Higgins JPT**, **Thomas J**, **Chandler J et al.**, *Cochrane Handbook for Systematic Reviews of Interventions version 6.2 (updated February 2021)*. Cochrane; 2021. Available from: www.training.cochrane.org/handbook

25 **Page MJ**, **McKenzie JE**, **Bossuyt PM et al**. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021; 372: n71

26 **Higgins JPT**, **Altman DG**, **Sterne JAC**. Chapter 8: Assessing risk of bias in included studies. In **Higgins JPT**, **Green S** eds, *Cochrane Handbook for Systematic Reviews of Interventions Version 510 (updated March 2011)*. The Cochrane Collaboration, 2011. Available from: www.handbook.cochrane.org

27 **Salanti G**, **Del Giovane C**, **Chaimani A**, **Caldwell DM**, **Higgins JPT**. Evaluating the quality of evidence from a network meta-analysis. *PLoS One* 2014; 9: e99682

28 **Veroniki AA**, **Vasiliadis HS**, **Higgins JPT**, **Salanti G**. Evaluation of inconsistency in networks of interventions. *Int J Epidemiol* 2013; 42: 332–45

29 **White IR**, **Barrett JK**, **Jackson D**, **Higgins JPT**. Consistency and inconsistency in network meta-analysis: model estimation using multivariate meta-regression. *Res Synth Methods* 2012; 3: 111–25

30 **Chaimani A**, **Higgins JPT**, **Mavridis D**, **Spyridonos P**, **Salanti G**. Graphical tools for network meta-analysis in STATA. *PLoS One* 2013; 8: e76654

31 **Veroniki AA**, **Straus SE**, **Fyraridis A**, **Tricco AC**. The rank-heat plot is a novel way to present the results from a network meta-analysis including multiple outcomes. *J Clin Epidemiol* 2016; 76: 193–9

32 **White IR**. Network meta-analysis. *Stata J* 2015; 15: 951–85

33 **Chaimani A**, **Salanti G**. Visualizing assumptions and results in network meta-analysis: the network graphs package. *Stata J* 2015; 15: 905–50

34 **Salanti G**, **Ades AE**, **Ioannidis JPA**. Graphical methods and numerical summaries for presenting results from multiple-treatment meta-analysis: an overview and tutorial. *J Clin Epidemiol* 2011; 64: 163–71

35 **Papakonstantinou T**, **Nikolakopoulou A**, **Higgins JPT**, **Egger M**, **Salanti G**. CINeMA: Software for semiautomated assessment of the confidence in the results of network meta-analysis. *Campbell Sys Rev* 2020; 16: e1080

36 **Nikolakopoulou A**, **Higgins JPT**, **Papakonstantinou T et al**. CINeMA: An approach for assessing confidence in the results of a network meta-analysis. *PLoS Medicine* 2020; 17: e1003082

37 **Yepes-Nuñez JJ**, **Li S-A**, **Guyatt G et al**. Development of the summary of findings table for network meta-analysis. *J Clin Epidemiol* 2019; 115: 1–13

38 **McVary KT**, **Gange SN**, **Gittelman MC et al**. Minimally invasive prostate convective water vapor energy ablation: a multicenter, randomized, controlled study for the treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia. *J Urol* 2016; 195: 1529–38

39 **Pisco JM**, **Bilhim T**, **Costa NV et al**. Randomised clinical trial of prostatic artery embolisation versus a sham procedure for benign prostatic hyperplasia. *Eur Urol* 2020; 77: 354–62

40 **Abt D**, **Hechelhammer L**, **Müllhaupt G et al**. Comparison of prostatic artery embolisation (PAE) versus transurethral resection of the prostate (TURP) for benign prostatic hyperplasia: randomised, open label, non-inferiority trial. *BMJ* 2018; 361: k2338

41 **Carnevale FC**, **Iscaife A**, **Yoshinaga EM**, **Moreira AM**, **Antunes AA**, **Srougi M**. Transurethral resection of the prostate (TURP) versus original and PErFecTED prostate artery embolization (PAE) due to benign prostatic hyperplasia (BPH): preliminary results of a single center, prospective, Urodynamic-controlled analysis. *Cardiovasc Intervent Radiol* 2016; 39: 44–52

42 **Gao Y-A**, **Huang Y**, **Zhang R et al**. Benign prostatic hyperplasia: prostatic arterial embolization versus transurethral resection of the prostate–a prospective, randomized, and controlled clinical trial. *Radiology* 2014; 270: 920–8

43 **Insausti I**, **Sáez de Ocáriz A**, **Galbete A et al**. Randomized comparison of prostatic artery embolization versus transurethral resection of the prostate for treatment of benign prostatic hyperplasia. *J Vasc Interv Radiol* 2020; 31: 882–90

44 **Radwan A**, **Farouk A**, **Higazy A**, **Samir YR**, **Tawfeek AM**, **Gamal MA**. Prostatic artery embolization versus transurethral resection of the prostate in management of benign prostatic hyperplasia. *Prostate Int* 2020; 8: 130–3

45 **Zhu C**, **Lin W**, **Huang Z**, **Cai J**. Prostate artery embolization and transurethral resection of prostate for benign prostatic hyperplasia: a prospective randomized controlled trial. *Chinese J Int Imaging Therapy* 2018; 15: 134–8

46 **Gratzke C**, **Barber N**, **Speakman MJ et al**. Prostatic urethral lift vs transurethral resection of the prostate: 2-year results of the BPH6 prospective, multicentre, randomized study. *BJU Int* 2017; 119: 767–75

47 **Roehrborn CG**, **Gange SN**, **Shore ND et al**. The prostatic urethral lift for the treatment of lower urinary tract symptoms associated with prostate enlargement due to benign prostatic hyperplasia: the L.I.F.T. Study. *J Urol* 2013; 190: 2161–7

48 **Chughtai B**, **Elterman D**, **Shore N et al**. The iTind temporarily implanted nitinol device for the treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia: a multicenter, randomized, Controlled Trial. *Urology* 2021; 153: 270–6

49 **Abbou CC**, **Payan C**, **Viens-Bitker C et al**. Transrectal and transurethral hyperthermia versus sham treatment in benign prostatic hyperplasia: a double-blind randomized multicentre clinical trial. The French BPH Hyperthermia. *Br J Urol* 1995; 76: 619–24

50 **Albala DM**, **Fulmer BR**, **Turk TMT et al**. Office-based transurethral microwave thermotherapy using the TherMatrx TMx-2000. *J Endourol* 2002; 16: 57–61

51 **Bdesha AS**, **Bunce CJ**, **Snell ME**, **Witherow RO**. A sham controlled trial of transurethral microwave therapy with subsequent treatment of the control group. *J Urol* 1994; 152(Pt 1): 453–8

52 **Blute ML**, **Patterson DE**, **Segura JW**, **Tomera KM**, **Hellerstein DK**. Transurethral microwave thermotherapy v sham treatment: double-blind randomized study. *J Endourol* 1996; 10: 565–73

53 **Brehmer M**, **Wiksell H**, **Kinn A**. Sham treatment compared with 30 or 60 min of thermotherapy for benign prostatic hyperplasia: a randomized study. *BJU Int* 1999; 84: 292–6

54 **De Wildt MJ**, **Hubregtse M**, **Ogden C**, **Carter SS**, **Debruyne FM**, **De la Rosette JJ**. A 12-month study of the placebo effect in transurethral microwave thermotherapy. *Br J Urol* 1996; 77: 221–7

55 **Larson TR**, **Blute ML**, **Bruskewitz RC**, **Mayer RD**, **Ugarte RR**, **Utz WJ**. A high-efficiency microwave thermoablation system for the treatment of benign prostatic hyperplasia: results of a randomized, sham-controlled, prospective, double-blind, multicenter clinical trial. *Urology* 1998; 51: 731–42

56 **Nawrocki JD**, **Bell TJ**, **Lawrence WT**, **Ward JP**. A randomized controlled trial of transurethral microwave thermotherapy. *Br J Urol* 1997; 79: 389–93

57 **Roehrborn CG**, **Preminger G**, **Newhall P et al**. Microwave thermotherapy for benign prostatic hyperplasia with the Dornier Urowave: results of a randomized, double-blind, multicenter, sham-controlled trial. *Urology* 1998; 51: 19–28

58 **Venn SN**, **Montgomery BS**, **Sheppard SA et al**. Microwave hyperthermia in benign prostatic hypertrophy: a controlled clinical trial. *Br J Urol* 1995; 76: 73–6

59 **Ahmed M**, **Bell T**, **Lawrence WT**, **Ward JP**, **Watson GM**. Transurethral microwave thermotherapy (Prostatron version 2.5) compared with transurethral resection of the prostate for the treatment of benign prostatic hyperplasia: a randomized, controlled, parallel study. *Br J Urol* 1997; 79: 181–5

60 **D'Ancona FC**, **Francisca EA**, **Witjes WP**, **Welling L**, **Debruyne FM**, **De La Rosette JJ**. Transurethral resection of the prostate vs high-energy thermotherapy of the prostate in patients with benign prostatic hyperplasia: long-term results. *Br J Urol* 1998; 81: 259–64

61 **Dahlstrand C**, **Waldén M**, **Geirsson G**, **Pettersson S**. Transurethral microwave thermotherapy versus transurethral resection for symptomatic benign prostatic obstruction: a prospective randomized study with a 2-year follow-up. *Br J Urol* 1995; 76: 614–8

62 **Floratos DL**, **Kiemeney LA**, **Rossi C**, **Kortmann BB**, **Debruyne FM**, **de La Rosette JJ**. Long-term followup of randomized transurethral microwave thermotherapy versus transurethral prostatic resection study. *J Urol* 2001; 165: 1533–8

63 **Nørby B**, **Nielsen HV**, **Frimodt-Møller PC**. Transurethral interstitial laser coagulation of the prostate and transurethral microwave thermotherapy vs transurethral resection or incision of the prostate: results of a randomized, controlled study in patients with symptomatic benign prostatic hyperplasia. *BJU Int* 2002; 90: 853–62

64 **Wagrell L**, **Schelin S**, **Nordling J et al**. Feedback microwave thermotherapy versus turp for clinical BPH—A randomized controlled multicenter study

65 **Parsons JK**, **Dahm P**, **Köhler TS**, **Lerner LB**, **Wilt TJ**. Surgical management of lower urinary tract symptoms attributed to benign prostatic hyperplasia: AUA guideline amendment 2020. *J Urol* 2020; 204: 799–804

66 **Dahm P**, **MacDonald R**, **McKenzie L**, **Jung JH**, **Greer N**, **Wilt T**. Newer minimally invasive treatment modalities to treat lower urinary tract symptoms attributed to benign prostatic hyperplasia. *Euro Urol Open Sci* 2021; 26: 72–82

67 **Miller LE**, **Chughtai B**, **Dornbier RA**, **McVary KT**. Surgical reintervention rate after prostatic urethral lift: systematic review and meta-analysis involving over 2,000 patients. *J Urol* 2020; 204: 1019–26

68 **Miller LE**, **Chughtai B**, **McVary K et al**. Water vapor thermal therapy for lower urinary tract symptoms secondary to benign prostatic hyperplasia: systematic review and meta-analysis. *Medicine* 2020; 99: e21365

69 **Svarc P**, **Taudorf M**, **Nielsen MB**, **Stroomberg HV**, **Røder MA**, **Lönn L**. Postembolization syndrome after prostatic artery embolization: a systematic review. *Diagnostics (Basel)* 2020; 10: 659

70 **Malde S**, **Umbach R**, **Wheeler JR et al**. A systematic review of patients' values, preferences, and expectations for the diagnosis and treatment of male lower urinary tract symptoms. *Eur Urol* 2021; 79: 796–809

71 **Dahm P**, **Franco J**. Re: A systematic review of patients' values, preferences, and expectations for the diagnosis and treatment of male lower urinary tract symptoms. *Eur Urol* 2021; 80: 254–5

72 **Salanti G**, **Dias S**, **Welton NJ et al**. Evaluating novel agent effects in multiple-treatments meta-regression. *Stat Med* 2010; 29: 2369–83

73 **Amparore D**, **De Cillis S**, **Volpi G et al**. First- and second-generation temporary implantable nitinol devices as minimally invasive treatments for BPH-related LUTS: systematic review of the literature. *Curr Urol Rep* 2019; 20: 47

74 **Jing J**, **Wu Y**, **Du M et al**. Urethral lift as a safe and effective procedure for prostatic hyplasia population: a systematic review and meta-analysis. *Front Surg* 2020; 7: 598728

75 **Knight GM**, **Talwar A**, **Salem R**, **Mouli S**. Systematic review and meta-analysis comparing prostatic artery embolization to gold-standard transurethral resection of the prostate for benign prostatic hyperplasia. *Cardiovasc Intervent Radiol* 2021; 44: 183–93

76 **Tallman CT**, **Zantek PF**, **Hernandez N**, **Morton RA Jr**, **Qi D**, **Gonzalez RR**. Effectiveness of convective water vapor energy therapy versus prostatic urethral lift for symptomatic benign prostatic hyperplasia: a systematic review and indirect comparison. *World J Urol* 2021; 39: 3207–15

77 **Tzeng M**, **Basourakos SP**, **Lewicki PJ**, **Hu JC**, **Lee RK**. New endoscopic in-office surgical therapies for benign prostatic hyperplasia: a systematic review. *Eur Urol Focus* 2021. In press. https://doi.org/10.1016/j.euf.2021.02.013

78 **Xiang P**, **Guan D**, **Du Z et al**. Efficacy and safety of prostatic artery embolization for benign prostatic hyperplasia: a systematic review and meta-analysis of randomized controlled trials. *Eur Radiol* 2021; 31: 4929–46

79 **Lokeshwar SD**, **Valancy D**, **Lima TFN**, **Blachman-Braun R**, **Ramasamy R**. A systematic review of reported ejaculatory dysfunction in clinical trials evaluating minimally invasive treatment modalities for BPH. *Curr Urol Rep* 2020; 21: 54

80 **Malling B**, **Røder MA**, **Brasso K**, **Forman J**, **Taudorf M**, **Lönn L**. Prostate artery embolisation for benign prostatic hyperplasia: a systematic review and meta-analysis. *Eur Radiol* 2019; 29: 287–98

81 **Tanneru K**, **Gautam S**, **Norez D et al**. Meta-analysis and systematic review of intermediate-term follow-up of prostatic urethral lift for benign prostatic hyperplasia. *Int Urol Nephrol* 2020; 52: 999–1008

82 **Hoffman RM**, **Monga M**, **Elliott SP et al**. Microwave thermotherapy for benign prostatic hyperplasia. *Cochrane Database Syst Rev* 2012; 2012: CD004135

83 **Tradewell MB**, **Albersheim J**, **Dahm P**. Use of the IDEAL framework in the urological literature: where are we in 2018? *BJU Int* 2019; 123: 1078–85

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Abbreviations: MD, mean difference; MIT, minimally invasive treatment; PAE, prostatic arterial embolization; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses; PUL, prostatic urethral lift; Q_{max}, maximum urinary flow rate; RCT, randomized controlled trial; RR, risk ratio; TIND, temporary implantable nitinol device; TUMT, transurethral microwave thermotherapy; WVTT, water vapour thermal therapy.