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Austrian Institute for
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Temporary nitinol implantation for the treatment of benign prostatic hyperplasia

Update 2025
Systematic Review

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Update 2025
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Project team

Project leader: Gregor Goetz, Dr.PH, MSSc, MPH

Authors: John Rathbone PhD
Ning Ma, MSPPM
Gregor Goetz, Dr.PH, MSSc, MPH

Project support

Systematic literature search: Tarquin Mittermayr, BA (Hons), MA

External Review: Prof. Dr. med. Rolf Muschter
Prim. Univ. Prof. Dr. Stephan Madersbacher

Internal Review: Dr. rer. soc. oec Ingrid Zechmeister-Koss, MA

Correspondence: Gregor Goetz, gregor.goetz@aihta.at

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Commissioned by the Austrian Ministry of Health, this report systematically assessed the intervention described herein as decision support for inclusion in the catalogue of benefits.

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Responsible for content:
Dr. rer.soc.oec. Ingrid Zechmeister-Koss, managing director

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List of abbreviations

AEs ..... adverse events
AUR ..... cute urinary retention
BOO..... bladder outlet obstruction
BPE ..... benign prostatic enlargement
BPH..... benign prostatic hyperplasia
BPO ..... benign prostatic obstruction
B-TUEP ..... enucleation with bipolar energy
B-TUERP..... bipolar transurethral enucleoresection
B-TURP ..... bipolar transurethral resection of the prostate
B-TUVP ..... bipolar transurethral electrovaporisation
DHT ..... dihydrotestosterone
DRE ..... digital rectal examination
EEP ..... endoscopic enucleation of the prostate
EUnetHTA ..... European Network for Health Technology Assessment
GRADE..... Grading of Recommendations, Assessment, Development and Evaluations
IIEF..... International Index of Erectile Function
IPSS..... International Prostate Symptom Score
LUTS ..... lower urinary tract symptoms
MCID..... minimal clinical important difference
M-TURP ..... monopolar transurethral resection of the prostate
OAB..... overactive bladder
OP..... open prostatectomy
PFR ..... peak urinary flow rate
PSA..... prostate-specific antigen
PVR ..... post-void residual volume
Qmax..... maximum urinary flow rate
QoL ..... quality of life
RCT..... randomised controlled trial
RoB 2..... Cochrane risk of bias 2
SAEs..... serious adverse events
SHIM ..... Sexual Health Inventory for Men
SUI ..... stress urinary incontinence
ThuLEP ..... thulium laser enucleation of the prostate
ThuVARP ..... thulium laser vaporesection of the prostate
ThuVEP ..... thulium laser vapoenucleation of the prostate
TIND..... temporary implantable nitinol device
TmLRP ..... thulium laser resection of the prostate
TUIP ..... transurethral incision of the prostate
TURP ..... transurethral resection of the prostate
WAVE ..... water vapor thermal therapy
WW ..... watchful waiting

Executive summary

Introduction

Health problem

Lower urinary tract symptoms (LUTS) in men refers to urinary symptoms commonly linked to bladder and prostate disorders, often due to benign prostatic hyperplasia (BPH). Symptoms fall into two categories: storage symptoms (frequency, urgency, nocturia, incontinence) and voiding symptoms (weak stream, straining, incomplete emptying). BPH as the primary cause of BPO results from BPE compressing the urethra, leading to bladder dysfunction, urinary retention and infections. If untreated, it may cause long-term damage. Treatment options include watchful waiting, medication and surgery.

LUTS in men: urinary symptoms often caused by BPH

long-term damages if untreated

several treatment options

Description of technology

The temporary implantable nitinol device (TIND) relieves BPH symptoms by reshaping the bladder neck and prostatic urethra to improve urine flow by pressure-necrosis induced atraumatic "incisions" in the 12, 5, and 7 o'clock positions. This minimally invasive procedure is performed under light sedation without catheterisation. The nitinol device, consisting of three struts and an anchoring leaflet, is inserted via cystoscopy and removed after five days under local anaesthesia. TIND is indicated for patients who prefer a minimally invasive alternative to traditional surgical procedures like transurethral resection of the prostate (TURP), those who want to preserve ejaculatory function due to its lower risk of sexual side effects compared to TURP, and individuals who are not ideal candidates for long-term medication (e.g. alpha blockers or 5-alpha reductase inhibitors) due to side effects or contraindications.

TIND: temporary nitinol implant; improves urine flow by reshaping the bladder neck and prostatic urethra

minimally invasive alternative to TURP

lower risk of sexual side effects, no long-term medication

Methods

A systematic search was conducted to evaluate the effectiveness and safety of TIND compared to standard care in patients with LUTS. Medline, Embase, Cochrane Library and CRD (DARE, NHS-EED, HTA) were searched from 2021 to 2024. The search was limited to articles published in English or German. Two authors independently conducted study selection, data extraction and quality appraisal. Any disagreements were resolved by a third author. The quality of the included studies was assessed using the Cochrane Risk of Bias 2 tool, and the certainty of the evidence was rated according to Grading of Recommendations, Assessment, Development and Evaluations (GRADE).

systematic search: TIND vs. standard care in pts. with LUTS

articles limited to English or German (2021-2024)

Cochrane RoB 2 tool, GRADE

Results

Available evidence

A total of one randomised controlled trial (RCT) and one single-arm study were included. The RCT provided only limited efficacy and safety data for TIND versus sham procedure and the single-arm study provided safety data for TIND.

1 RCT and 1 single-arm study: limited efficacy and safety data

Clinical effectiveness and safety

TIND vs sham

The RCT assessed functional outcomes at three months, finding that 78.6% of TIND patients achieved an International Prostate Symptoms Score (IPSS) reduction of ≥3 points (minimal clinical important difference, MCID), compared to 60% in the sham group, which was a statistically significant difference. At three months, the IPSS quality-of-life (QoL) score was not significantly different between TIND and sham groups. At three months, the mean difference in Qmax and PVR scores significantly favoured TIND compared to sham. At three months, the mean difference in Sexual Health Inventory for Men (SHIM) and International Index of Erectile Function (IIEF) scores were not significantly different between TIND and sham.

RCT 3-month result showed improvement for TIND for IPSS, QoL, Qmax and PVR

SHIM and IIEF: no significant difference between groups

Adverse events were more frequent in the TIND group (109 events from 45 participants) compared to the sham group (19 events from 10 participants). Within 30 days, 38% of TIND patients experienced at least one adverse event, compared to 18% in the sham group. Serious adverse events occurred in 7.8% of TIND patients (16 events from 10 participants) versus 3.5% in the sham group (two events from two participants). One death occurred in the TIND arm and no deaths in the sham arm. The cause of death was not reported.

more adverse events were observed for TIND pts.

one death in TIND group, no deaths in sham group

cause not reported

Common adverse events in the TIND group included dysuria (22.9%), haematuria (13.6%), micturition urgency (5.1%), pollakisuria (6.8%), urinary retention (5.9%), and urinary tract infection (1.7%), while these were less frequent or absent in the sham group. Sepsis and pain were each reported in one patient in the TIND group, with no cases in the sham group.

common adverse events (TIND): dysuria, haematuria, urgency, pollakisuria, retention, UTI

TIND single-arm study

Adverse events reported in the single-arm study found that haematuria occurred in 12.3% of patients, while micturition urgency was observed in 11.1%. Pain and urinary retention were each reported in 9.9% of participants, and dysuria in 7.4%. Urinary tract infections were noted in 6.2%, while an increase in voiding symptoms was seen in 1.2% of patients.

single arm study also flagged adverse events for TIND pts.

Upcoming evidence

Currently, there are no ongoing RCTs directly comparing TIND with any of the standard Operations of BPH (TURP, endoscopic enucleation of the prostate (EEP), or open prostatectomy (OP). Instead, ongoing clinical trials primarily focus on comparing TIND to UroLift and Rezūm, which are minimally invasive alternatives. Due to the absence of direct comparative data with TURP or OP, a re-evaluation of TIND's clinical effectiveness and safety in relation to standard care is not currently recommended. Future studies directly comparing TIND to these established surgical treatments will be necessary to determine its long-term efficacy and role in clinical practice.

no ongoing RCTs directly comparing TIND vs. standard operations

ongoing trials: TIND vs. other minimally invasive treatment options such as Urolift and Rezūm

Discussion

The methodology of this review has several strengths, primarily due to its systematic approach and rigorous search strategy. A comprehensive literature search, combined with an independent review of studies by two reviewers, enhances confidence that the included studies accurately represent the available evidence.

strong and systematic review methodologies: literature search, independent review

limitations due to evidence ability and maturity

no direct comparisons with TURP, EEP, or OP

evidence still emerging

follow-up only 3 months need for long-term studies

However, this review also has notable limitations. The direct comparisons between TIND and its comparators (i.e. TURP, EEP or OP) is absent from the evidence base. While it limits the ability to draw any direct conclusion for this comparison, it also implies the differences between TIND, as the minimally invasive procedure, and other more established surgical options. Evidence on the comparison between TIND and other minimum invasive procedures are still emerging. Therefore, the comparison to the sham procedure and its finding from the trial is appropriate to support the conclusion of this review. Additionally, the trial outcomes reported data at only three months, providing limited insight into the long-term durability of treatment effects. These limitations highlight the need for longer-term studies to investigate how TIND could contribute to the overall management of the disease.

Conclusion

with low certainty evidence and inferior safety: TIND is unlikely to change the current clinical practice

One RCT with a small sample size assessed the safety and effectiveness of TIND compared to a sham procedure in patients with LUTS. However, the evidence is of very low certainty, with short-term follow-up providing no clear long-term evidence on the safety or efficacy of TIND. Adverse events were more frequent in the TIND group than in the sham group. The single-arm study of TIND reported generally higher incidence of adverse events than the RCT. Based on the best available evidence, TIND is unlikely to significantly change how patients are managed, and the standard of care is still considered the mainstay.

Zusammenfassung

Einleitung

Indikation und therapeutisches Ziel

benigne Prostatahyperplasie (BPH) häufige Erkrankung des alternden Mannes

Die benigne Prostatahyperplasie (BPH) ist eine häufige Erkrankung des alternden Mannes, die durch eine Vergrößerung der Prostata gekennzeichnet ist. Diese Vergrößerung kann zu einer Obstruktion der Harnröhre führen und untere Harnwegssymptome (lower urinary tract symptoms, LUTS) verursachen. Zu den typischen LUTS gehören:

- *Speichersymptome:* Häufiges Wasserlassen, verstärkter Harndrang, nächtliches Wasserlassen und unfreiwilliger Harnverlust (Inkontinenz).
- *Entleerungssymptome:* Abgeschwächter Harnstrahl, Schwierigkeiten beim Beginn der Miktion, Pressen beim Wasserlassen und das Gefühl der unvollständigen Blasenentleerung.

unbehandelt können schwere Komplikationen auftreten

LUTS können die Lebensqualität der Betroffenen erheblich beeinträchtigen und unbehandelt zu Komplikationen wie Harnverhalt, Harnwegsinfektionen, Blasensteinen und Nierenschäden führen. Die Prävalenz von BPH und LUTS nimmt mit dem Alter deutlich zu.

therapeutisches Ziel: Symptomlinderung und Komplikationsvermeidung

Das therapeutische Ziel der BPH-Behandlung besteht darin, die Symptome zu lindern, die Lebensqualität zu verbessern und Komplikationen vorzubeugen. Die Behandlungsoptionen reichen von beobachtendem Zuwarten (Watchful Waiting) über medikamentöse Therapie bis hin zu chirurgischen Eingriffen.

Beschreibung der Technologie

TIND: minimal-invasives temporäres Nitinol-Implantat

TIND ist ein minimal-invasives, temporäres Implantat aus Nitinol (Nickel-Titan-Legierung). Es wird zystoskopisch in die prostatische Harnröhre eingebracht, expandiert dort und übt radialen Druck aus, um den Harnabfluss zu verbessern. Das TIND (bzw. iTIND der zweiten Generation mit optimiertem Design) wird nach 5-7 Tagen unter Lokalanästhesie entfernt. Es ist keine Katheterisierung erforderlich.

Fragestellung

Forschungsfrage

Ist die perkutane temporäre Nitinol-Implantation (TIND) im Vergleich zur bestmöglichen Standardtherapie (z. B. transurethralen Resektion der Prostata (TURP) oder offenen Prostatektomie) bei der Behandlung von LUTS hinsichtlich patientenrelevanter Endpunkte wie International Prostate Symptom Score (IPSS) und unerwünschten Ereignissen wirksamer und gleich sicher?

Methoden

systematische Literatursuche in 4 Datenbanken

Es wurde eine umfassende systematische Literatursuche in den Datenbanken Medline (via Ovid), Embase, Cochrane Library und CRD (von 2021 bis 2024) durchgeführt. Ergänzend erfolgte eine Suche in relevanten Studienregistern, um laufende oder unveröffentlichte Studien zu identifizieren.

Zwei Wissenschaftler waren in alle Schritte des Review-Prozesses involviert. Dies umfasste die unabhängige Auswahl relevanter Studien anhand vordefinierter Einschlusskriterien, die Extraktion von Daten aus klinischen Studien, sowie die Bewertung des Verzerrungspotenzials innerhalb der eingeschlossenen Studien (unter Verwendung des Cochrane RoB 2 Tools für RCTs). Die Gesamtqualität der Evidenz für jeden Endpunkt wurde mithilfe des GRADE-Ansatzes bewertet

Studienauswahl, Extraktion & Qualitätsbewertung durch 2 Forscher

Klinische Wirksamkeit

Für die Bewertung der Wirksamkeit wurden randomisierte kontrollierte Studien (RCTs) berücksichtigt, die TIND direkt mit TURP oder offener Prostatektomie verglichen. Folgende Endpunkte wurden dabei als entscheidungsrelevant definiert:

entscheidungsrelevante Endpunkte für klinische Wirksamkeit

- International Prostate Symptom Score (IPSS),
- maximaler Harnfluss (Qmax),
- Restharnvolumen (PVR),
- Reinterventionsrate,
- BPH Impact Index,
- generische und krankheitsspezifische Lebensqualitätsmaße,
- persistierende irritative Symptome und postoperative LUTS

Sicherheit

Zur Bewertung der Sicherheit wurden zusätzlich zu den RCTs auch prospektive, nicht-randomisierte kontrollierte Studien sowie prospektive Fallserien mit einer Mindestteilnehmerzahl von 50 Patienten eingeschlossen. Unerwünschte und schwerwiegende Unterwünschte Ereignisse wurden dabei als entscheidungsrelevante Endpunkte definiert.

entscheidungsrelevante Endpunkte für Sicherheit

Ergebnisse

Verfügbare Evidenz

Insgesamt erfüllten ein RCT, der TIND mit einem Scheinverfahren (Sham) verglich, und eine einarmige prospektive Studie die Einschlusskriterien. Der multizentrische RCT verglich TIND mit einem Scheinverfahren bei 185 Teilnehmern mit einem Durchschnittsalter von 61 Jahren. Die Studie wurde in den USA und Kanada durchgeführt. Die Einschlusskriterien umfassten einen IPSS ≥10, maximalen Harnfluss ≤12 mL/sec und ein Prostatavolumen zwischen 25-75 cc. Die Nachbeobachtung erfolgte verblindet über 3 Monate mit anschließender unverblindeter Phase bis 12 Monate. Die Abbruchquote betrug etwa 30 %. In der einarmigen Studie wurden 81 Personen eingeschlossen (medianes Alter: 65 Jahre) und über 12 Monate nachbeobachtet. Die Abbruchquote betrug 12,3 %.

1 RCT und 1 einarmige Studie

Vertrauenswürdigkeit der Evidenz

Die Vertrauenswürdigkeit der gesamten Evidenz wurde nach GRADE als sehr niedrig eingestuft. Dies begründet sich vor allem durch das hohe Verzerrungspotenzial aufgrund der hohen Studienabbruchquote (etwa 30 %), die indirekte Evidenz durch den Vergleich mit einem Scheinverfahren statt der Standardtherapie (TURP oder Prostatektomie) sowie die Ungenauigkeit der Effektschätzung aufgrund der kleinen Studienpopulation (n=185) und breiter Konfidenzintervalle.

GRADE: sehr niedrige Vertrauenswürdigkeit der Evidenz

Klinische Wirksamkeit

Wirksamkeit: IPSS-Reduktion bei 79 % vs. 60 %

In der randomisierten kontrollierten Studie erreichten nach 3 Monaten 78,6 % der TIND-Patienten eine **IPSS-Reduktion** von ≥3 Punkten, verglichen mit 60 % in der Kontrollgruppe. Der Unterschied war statistisch signifikant (RR 1,31; 95 % CI 1,04 bis 1,65).

Verbesserung von Harnfluss und Restharn

Der **maximale Harnfluss** (Qmax) verbesserte sich in der TIND-Gruppe signifikant mit einer mittleren Differenz von 2,15 mL/s (95 % CI 0,38 bis 3,92). Beim **Restharnvolumen** (PVR) zeigte sich eine mittlere Differenz von -7,46 mL (95 % CI -26,98 bis 12,06).

keine Unterschiede bei Sexualfunktion und Lebensqualität

Bei der **Lebensqualität** (IPSS-QoL) und sexuellen Funktion (SHIM: MD 3,02; 95 % CI -4,04 bis 10,08) zeigten sich keine signifikanten Unterschiede zwischen den Gruppen.

fehlende Daten zu weiteren definierten Endpunkten

Für die vorab definierten Endpunkte **Reinterventionsrate**, **BPH Impact Index, persistierende irritative Symptome und postoperative LUTS** wurden keine Ergebnisse berichtet.

Sicherheit

mehr unerwünschte Ereignisse in TIND-Gruppe

Die TIND-Gruppe wies mehr **unerwünschte Ereignisse** auf (RR 1,27; 95 % CI 0,97 bis 1,67; entspricht 513 zusätzlichen Komplikationen pro 1.000 Patienten, wobei die tatsächliche Anzahl zwischen 57 weniger und 1.000 mehr schwanken könnte). Innerhalb von 30 Tagen traten bei 38 % der TIND-Patienten unerwünschte Ereignisse auf (vs. 18 %).

schwerwiegende Ereignisse dokumentier

Schwerwiegende unerwünschte Ereignisse wurden bei 7,8 % der TIND-Patienten dokumentiert vs. 3,5 % in der Kontrollgruppe (RR 2,42; 95 % CI 0,51 bis 11,41). Die häufigsten Komplikationen in der TIND-Gruppe waren Dysurie (22,9 %), Hämaturie (13,6 %), Pollakisurie (6,8 %) und Harnverhalt (5,9 %).

Ergebnisse der einarmigen Studie

In der einarmigen Studie wurden folgende unerwünschte Ereignisse beobachtet: Hämaturie bei 12,3 % (n=10) der Patienten, Harndrang (Micturition urgency) bei 11,1 % (n=9), Schmerzen und Harnverhalt bei jeweils 9,9 % (n=8) sowie Dysurie bei 7,4 % (n=6) der Teilnehmer. Harnwegsinfektionen traten bei 6,2 % (n=5) auf und eine Zunahme der Entleerungssymptome wurde bei 1,2 % (n=1) der Patienten festgestellt. Die Komplikationen waren selbstlimitierend und traten mehrheitlich kurzfristig auf (54,7 % ≤7 Tage; 30,2 % 8-20 Tage; 15,1 % 20-30 Tage).

Therapieversagen bei 5 % der Patienten

In der einarmigen Studie wurde zudem ein Therapieversagen (Treatment Failure Rate) bei 5 % (4/81 Patienten) berichtet.

Laufende Studien

3 laufende RCTs

In den Studienregistern sind derzeit drei RCTs dokumentiert: eine Studie vergleicht TIND mit einem Scheinverfahren bei 279 Patienten zur Bewertung der Sicherheit, eine zweite Studie untersucht TIND gegen UroLift (n=206) mit Fokus auf Komplikationen, und eine dritte Studie (n=20) vergleicht TIND mit Rezūm hinsichtlich der IPSS-Veränderung. Derzeit läuft keine Studie, die TIND direkt mit den Standardverfahren TURP oder offener Prostatektomie vergleicht. Die Studien sollen zwischen 2024 und 2025 abgeschlossen werden.

Diskussion und Schlussfolgerung

Die Evidenz für TIND ist aufgrund methodischer Limitationen der Studien (kurzes Follow-up, Verzerrungsrisiko) und des Fehlens direkter Vergleiche mit der etablierten Standardtherapie sowie fehlender Langzeitdaten von sehr niedriger Vertrauenswürdigkeit. Sicherheitsbedenken bestehen aufgrund der höheren Rate unerwünschter Ereignisse im Vergleich zum Scheinverfahren.

sehr niedrige Vertrauenswürdigkeit der Evidenz

In Ermangelung belastbarer vergleichender Daten sind daher keine Schlussfolgerungen zur komparativen klinischen Wirksamkeit von TIND im Vergleich zur Standardtherapie möglich. Eine Neubewertung wird erst bei Vorliegen aussagekräftiger, qualitativ hochwertiger Studien mit direkten Vergleichen empfohlen.

Evidenz unzureichend

1 Background

Update des EUnetHTA-Berichts von 2021

This report represents an update of the 2021 EUnetHTA report that evaluated the effectiveness and safety of multiple surgical techniques and devices for benign prostatic hyperplasia (BPH) [1]. At the time of the EUnetHTA report publication, no randomised controlled trials (RCTs) were available for TIND. The findings were based on the OTCA27 report, 'Comparative effectiveness of surgical techniques and devices for the treatment of benign prostatic hyperplasia' [1]. In this update assessment, we focus on temporary implantable nitinol device (TIND) versus transurethral resection of the prostate (TURP) monopolar or bipolar and open prostatectomy (OP) or adenomectomy.

1.1 Health problem and characteristics of the technology

Overview of the disease or health condition and target population[1,2]

untere Harnwegssymptome (LUTS) bei Männern: oft durch benigne Prostatahyperplasie verursacht

The term 'lower urinary tract symptoms' (LUTS) in males is broad and non-specific. It can refer to any combination of urinary symptoms or be used more specifically to describe symptoms commonly linked to an overactive bladder, such as increased frequency, urgency and nocturia. LUTS describe the urinary abnormalities shared by disorders affecting the bladder and prostate, typically caused by benign prostatic hyperplasia (BPH). LUTS are a common issue in men, particularly as they age. When BPH causes these symptoms, they can significantly impact quality of life. Males with LUTS may report one or any combination of symptoms that typically fluctuate over time and may remit spontaneously. LUTS can be categorised into two main types:

- **Storage symptoms:** (frequency, urgency, nocturia and incontinence) [2-4]
- **Voiding symptoms:** (difficulty starting urination, a weak urine stream, straining to urinate and a feeling of incomplete bladder emptying) [2-6]

benigne Prostatahyperplasie (BPH) als Hauptursache: Prostatavergrößerung komprimiert Harnröhre

The primary cause of LUTS is BPH, a non-malignant enlargement of the prostate gland that compresses the urethra and obstructs urine flow. This can lead to bladder dysfunction over time. BPH involves the proliferation of stromal and epithelial cells in the prostate's transition zone, causing urethral compression and bladder outflow obstruction. This can lead to LUTS, urinary retention, infections and potentially life-threatening chronic high-pressure retention with long-term bladder damage if untreated [7]. Treatment options include watchful waiting (WW), medical therapy and surgical interventions.

[1] **A0002** – What is the disease or health condition in the scope of this assessment?

[2] **A0007** – What is the target population in this assessment?

LUTS nicht nur durch Prostataprobleme: auch Blasenfunktionsstörungen oder Entzündungen können Ursache sein

LUTS have traditionally been linked to bladder outlet obstruction, often resulting from benign prostatic enlargement (BPE) subsequently followed by benign prostatic obstruction (BPO). However, research increasingly shows that LUTS may also arise from non-prostatic causes, including bladder dysfunction (e.g. detrusor overactivity, underactivity or other urinary tract abnormalities) and prostatic inflammation. Additionally, non-urological conditions, particularly nocturia, can contribute to LUTS [8].

Lower urinary tract symptoms risk factors and disease course[3,4]

Risikofaktoren für LUTS und BPH: Alter, Diabetes, Entzündungen, Übergewicht und metabolisches Syndrom

Risk factors include non-modifiable factors (e.g. age, genetics and geography) and modifiable factors like diabetes, localised inflammation, obesity, hypertension and metabolic syndrome [9-11]. Age is a significant predictor of the development of BPH and subsequent LUTS. Fifty per cent of men older than 50 show evidence of BPH, and the association with the development of LUTS increases linearly with age. Diabetes mellitus is recognised as a risk factor for LUTS, although the presence of urinary symptoms is not directly related to the degree of glycaemic control. This association is particularly strong in younger males (under 70 years old) and those with longstanding diabetes (more than five years) [12]. Other conditions linked to LUTS include cardiovascular disease and a sedentary lifestyle.

natürlicher Verlauf: oft langsame Progression mit steigendem Risiko für akuten Harnverhalt

The natural course of LUTS depends on the underlying cause, but in general, LUTS associated with conditions like BPH or other ageing-related changes often progresses gradually. The progression of LUTS has been found in up to 31% of men with BPH over a seven-year follow-up period [13]. While progression to acute urinary retention is less common, its incidence varies with age. Among men with moderate symptoms, the rate ranges from 3.0 per 1,000 person-years for those aged 40 to 49, to 34.7 per 1,000 person-years for those aged 70 to 79 [13]. BPH significantly impacts public health and individual quality of life [14],[15]. In Europe, 30% of men over 50 years of age – equivalent to approximately 26 million men – experience LUTS.

Effects of the disease or health condition on the individual and society[5,6]

Belastung durch körperliche Beschwerden und Einschränkungen im Alltag

The burden of disease for patients with LUTS is significant and multifaceted, affecting their physical, mental and social wellbeing. LUTS can lead to discomfort, embarrassment and disruptions in daily activities, ultimately reducing overall quality of life. Additionally, patients may experience comorbidities such as chronic kidney disease, depression and prostatitis.

gesellschaftliche Folgen: Produktivitätsverluste und psychosoziale Belastungen

Beyond individual health, LUTS has broader societal consequences. Frequent bathroom breaks, discomfort and sleep disturbances can disrupt work life, reducing productivity and increasing absenteeism. The psychological and social impact is also profound, as individuals with LUTS often face anxiety, depression and social isolation due to the stigma and inconvenience of their symptoms [16].

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[3] **A0003** – What are the known risk factors for the disease or health condition

[4] **A0004** – What is the natural course of the disease or health condition?

[5] **A0005** – What is the burden of disease for patients with the disease or health condition?

[6] **A0006** – What are the consequences of the disease or health condition for the society?

Target population[7,8,9]

Zielgruppe: Männer mit LUTS durch BPH

The target condition is men (>18 years of age) with LUTS attributed to BPH. Either prostate weight or size will be used to define three relevant subpopulations often identified in guidelines (prostate size <30 mL, 30-80 mL and >80 mL).

Prävalenz: steigende Häufigkeit mit dem Alter, bis zu 90 % aller Männer über 70 betroffen

Differences in definitions make the interpretation of population-based studies regarding BPH difficult. For example, BPH can refer to histology, prostate enlargement, prostatic glandular hypertrophy, bladder outlet obstruction or just a physician's diagnosis of BPH [11]. Disease prevalence has been shown to increase with advancing age. The histological prevalence of BPH at autopsy is as high as 50% to 60% for males in their 60s, increasing to 80% to 90% of those older than 70 years of age [11, 17]. A population study in men in Poland found LUTS present in 66.2% of men aged ≥ 40 years [18], whereas studies in men from Taiwan found LUTS ranged from 34% to 50% in those aged ≥ 40 years [19]. The burden of benign prostatic hyperplasia is rising throughout the world, primarily due to population growth and ageing. Globally, there were 94 million prevalent cases of BPH in 2019, compared with 51·1 million cases in 2000 [20]. Consequently, the male burden on the existing healthcare system is expected to grow substantially in the coming years.

Prävalenz in Österreich: 64,6 % der Männer zwischen 15-89 Jahren von LUTS betroffen

A population-based cross-sectional survey on LUTS was conducted in 2009 in Austria. Some degree of LUTS was reported in 64.6% of the male population aged from 15 to 89 years. In all age groups, storage symptoms are more prevalent than voiding symptoms. The prevalence of voiding symptoms (IPSS >0) among Austrian males is 35.5%, and the prevalence of storage symptoms is 61.6% [21]. According to information provided by the submitting hospitals, the annual utilisation of TIND in Austria is estimated to be 300 new cases each year.

Current clinical management of the disease or health condition[10,11]

Diagnostik: Anamnese, körperliche Untersuchung, Urinanalyse und PSA-Test zur Unterscheidung von Prostatakrebs

According to the European Association of Urology, the initial evaluation of LUTS suggestive of BPH involves several steps. These include taking a comprehensive patient history, conducting a physical examination with a digital rectal examination (DRE), performing a urinalysis and ordering a prostate-specific antigen (PSA) blood test if prostate cancer diagnosis would alter management. Additional tools, such as a voiding diary and the International Prostate Symptom Score (IPSS) to investigate urodynamics and secondary health conditions, are also used [8] [22].

Watchful waiting

beobachten und abwarten oft ausreichend bei milden bis moderaten Symptomen

Many men with mild-to-moderate LUTS do not require or desire drugs or surgical treatment. All men should be assessed to determine symptom severity and differentiate uncomplicated from complicated LUTS for surgical indications. Watchful waiting (WW) is a viable option for men with non-both-

[7] **A0007** – What is the target population in this assessment?

[8] **A0023** – How many people belong to the target population?

[9] **A0011** – How much are the technologies utilised?

[10] **A0024** – How is the disease or health condition currently diagnosed according to published guidelines and in practice?

[11] **A0025** – How is the disease or health condition currently managed according to published guidelines and in practice?

ersome LUTS, as most remain stable for years, with minimal risk of progression to acute urinary retention (AUR) or complications [23-25]. In one study, 85% of men with mild LUTS remained stable on WW after one year [26]. A comparison of WW and TURP in men with moderate LUTS showed improved bladder function in the surgical group, but 64% of WW patients remained stable over five years, with 36% transitioning to surgery [27], [28] [149, 150]. Increasing symptom bother, and PVR volumes are key predictors of WW failure. WW is suitable for men with mild-to-moderate uncomplicated LUTS who are not significantly troubled by symptoms.

Behavioural and dietary modifications

konservatives Management: Aufklärung, Lebensstiländerungen und regelmäßige Kontrollen

Management typically includes education about the patient's condition and reassurance that their urinary symptoms are not caused by cancer. Regular monitoring and lifestyle advice are essential components. Lifestyle changes may involve reducing fluid intake at specific times to minimise urinary frequency during inconvenient periods (e.g. at night or in public). Patients are advised to moderate caffeine and alcohol intake due to their diuretic and irritant effects, which can exacerbate frequency, urgency and nocturia. Relaxed and double-voiding techniques and urethral milking can help prevent postmicturition dribble [8].

weitere Strategien: Ablenkungstechniken, Blasentraining und Medikationsanpassung

Additional strategies include distraction techniques (e.g. penile squeeze, breathing exercises or mental tricks to take the mind off the bladder) to manage overactive bladder (OAB) symptoms and bladder retraining to increase capacity and time between voids. Reviewing and adjusting medications, especially diuretics, to minimise urinary side effects is also important. Assistance may be provided for those with impaired dexterity, mobility or mental state, and addressing constipation is recommended to improve symptoms [8].

Pharmacological treatment

pharmakologische Therapie:

α1-Adrenoceptor antagonists (α1-blockers)

α1-Blocker: verbessern Harnfluss, keine Wirkung auf Prostatavolumen oder Progression

Treatment for men with moderate-to-severe LUTS caused by BOO due to an enlarged prostate includes alpha blockers (e.g. tamsulosin, alfuzosin, silodosin, doxazosin, terazosin), which relax smooth muscle in the prostate and bladder neck to improve urine flow [8].

Alpha reductase inhibitors (5-ARIs)

5-ARIs: senken Prostatavolumen, wirksam bei Progression

Treatment for men with LUTS and evidence of prostate enlargement (prostate volume >40 mL or PSA >1.5 ng/mL) includes alpha-reductase inhibitors (5-ARIs) (e.g. finasteride, dutasteride), which reduce prostate size by inhibiting dihydrotestosterone (DHT) production [8].

Muscarinic receptor antagonists

Muskarinrezeptor-antagonisten: für überaktive Blase, Risiko von Harnverhalt bei Prostatavergrößerung

Treatment for men with overactive bladder symptoms (e.g. urgency, frequency) without significant post-void residual (PVR) volume includes muscarinic receptor antagonists (e.g. oxybutynin, tolterodine, solifenacin), which reduce detrusor overactivity by inhibiting muscarinic receptors [8].

Beta-3 adrenergic agonists

Beta-3-Agonisten: für überaktive Blase

Treatment for men with overactive bladder symptoms who cannot tolerate or have contraindications to antimuscarinics includes beta-3 adrenergic agonists (e.g. mirabegron), which relax the detrusor muscle during the storage phase to functionally increase bladder capacity [8].

Phosphodiesterase-5 (PDE5) inhibitors

Treatment for men with LUTS and erectile dysfunction includes phosphodiesterase-5 (PDE5) inhibitors (e.g. tadalafil), which improve LUTS by relaxing the smooth muscle in the bladder, prostate and pelvic vasculature [8].

PDE5-Hemmer: verbessern LUTS und erektile Dysfunktion durch Muskelrelaxation

Medical therapies for LUTS primarily focus on relieving the symptoms associated with conditions, though each class has potential limitations and side effects. When the medical treatment reached its ceiling effects or patients are unsatisfied with the efficacy, surgical management is considered [29].

medikamentöse Therapie: primär für Symptomlinderung …

Surgical treatment of benign prostatic obstruction

The European Association of Urology states that surgical treatment is a fundamental component of LUTS/BPO management [8]. Surgical treatment is recommended for men with LUTS due to BPO under specific conditions and can include resection, enucleation, vaporization, alternative ablative techniques, and non-ablative techniques:

… bei unzureichender Wirksamkeit chirurgische Intervention erwägen

Resection of the prostate

TURP can be performed as monopolar (M-TURP) or bipolar (B-TURP). It removes tissue from the prostate's transition zone, reducing prostate volume and PSA by 25-58%. M-TURP is effective for moderate-to-severe LUTS caused by BPO and is suitable for prostates sized 30-80 mL [8].

TURP: entfernt Prostatagewebe, 25-58 % Volumenreduktion, für Prostatavolumen 30-80 ml

Thulium:yttrium-aluminium-garnet laser vaporesection of the prostate

In the thulium:yttrium-aluminium-garnet laser (Tm: YAG), a wavelength between 1,940 and 2,013 nm is emitted in continuous wave mode. The laser is primarily used in front-fire applications. Laser vaporesection of the prostate using Tm:YAG laser (ThuVARP) has similar operation, catheterisation and hospitalisation times compared to TURP. ThuVARP and TURP are equivalent in terms of IPSS, but not Qmax, with TURP deemed superior at 12 months follow-up. ThuVARP and TURP show similar short-term safety. Mid- to long-term results on efficacy and safety compared to TURP are very limited [8].

Thulium-Laser-Vaporesektion der Prostata

Transurethral incision of the prostate

Transurethral incision of the prostate (TUIP) involves incising the bladder outlet without relevant tissue removal. Transurethral incision of the prostate is conventionally performed with a Collins knife using electrocautery. However, alternative energy sources such as holmium laser may be used. The mainstay of this technique is in prostate sizes <30 mL without a middle lobe. Transurethral incision of the prostate shows similar efficacy and safety to M-TURP for treating moderate-to-severe LUTS secondary to BPO in men with prostates < 30 mL [8].

TUIP: Inzision des Blasenhalses, keine Resektion"

Enucleation of the prostate

Open prostatectomy

OP is a relatively old surgical treatment for moderate-to-severe LUTS secondary to BPO. Obstructive adenomas are enucleated using the index finger, approaching from within the bladder (Freyer procedure) or through the anterior prostatic capsule (Millin procedure). It is used for substantially enlarged glands (>80-100 mL). OP is the most invasive surgical method, but it is an effective and durable procedure for the treatment of LUTS/BPO [8].

offene Prostatektomie chirurgische Standardtherapie

Bipolar transurethral enucleation of the prostate

Bipolare transurethrale Enukleation

Following the principles of bipolar technology, the obstructive adenoma is enucleated endoscopically by the transurethral approach. Currently, two technologies exist, namely plasmakinetic (PK) enucleation of the prostate (PKEP) and bipolar plasma enucleation of the prostate (BPEP). Bipolar transurethral enucleation of the prostate is followed by either morcellation or resection of the enucleated adenoma [8].

Holmium laser enucleation of the prostate

HoLEP: Holmium-Laser-Enukleation der Prostata

The holmium:yttrium-aluminium garnet (Ho: YAG) laser (wavelength 2,140 nm) is a pulsed solid-state laser that acts through phtothermal mechanism to rapid vaporase tissues which leads to tissue coagulation. Tissue coagulation and necrosis are limited to 3-4 mm, which is enough to obtain adequate haemostasis [8].

Thulium:yttrium-aluminium-garnet laser enucleation of the prostate

ThuVEP/ThuLEP: Thulium-Laser-Enukleation

Enucleation using the Tm: YAG laser includes thulium vapoenucleation of the prostate (ThuVEP) and thulium laser enucleation of the prostate (ThuLEP) (blunt enucleation). Super pulsed or continuous wave thulium:yttrium-aluminium garnet (wavelength 2,013 nm) or thulium fibre lasers (wavelength 1,940 nm) are used for laser enucleation of the prostate and are well absorbed by water and water-containing tissues [8].

Diode laser enucleation of the prostate

Diodenlaser: Vaporisation/Enukleation der Prostata

For prostate surgery, diode lasers with a wavelength of 940, 980, 1,318 and 1,470 nm (depending on the semiconductor used) are marketed for vaporisation and enucleation. Only a few have been evaluated in clinical trials [8].

Vaporisation of the prostate

Bipolar transurethral vaporisation of the prostate

B-TUVP: Bipolare transurethrale Vaporisation

Bipolar transurethral vaporisation of the prostate (B-TUVP) utilises a bipolar electrode and a high-frequency generator to create a plasma field (thin layer of highly ionised particles) to vaporise prostatic tissue. Bipolar transurethral vaporisation of the prostate displays thinner (<2 mm) coagulation zones, compared to monopolar TUVP (up to 10 mm), potentially resulting in fewer irritative side effects and stress urinary incontinence (SUI) [8].

532 nm (GreenLight) laser vaporisation of the prostate

GreenLight-Laser: In-situ-Vaporisation

Two approaches exist for potassium-titanyl-phosphate (KTP) and the lithium triborate (LBO) laser-based enucleation technique. GreenLEP is an anatomical enucleation technique following the principle of blunt dissection of the adenoma with the sheath and laser energy for incision as described for ThuLEP. A variation is the in situ vaporisation of apically enucleated tissue, also referred to as the anatomic vaporisation-incision technique. To date, no high-quality adequate RCTs evaluating enucleation using the KTP/LBO laser have been carried out [8].

Technological features of the intervention[12]

TIND: Minimal-invasive BPH-Intervention

TIND is a minimally invasive intervention for LUTS due to BPH. TIND aims to alleviate the symptoms of BPH by creating new channels in the urethra, thereby improving urine flow. This procedure can be performed in an outpatient setting under light sedation. Using cystoscopy, the device is inserted into the prostatic urethra, where it is expanded upon deployment, reshaping the bladder neck and prostatic urethra [30]. Notably, this approach does not require catheterisation. The TIND is a 50-mm-long, 33-mm-diameter device composed of three elongated struts and an anchoring leaflet, all constructed from nitinol – a biocompatible, super-elastic shape-memory alloy [30]. The device is self-expanding and is placed in the prostatic urethra and bladder neck. It typically remains in situ for five to seven days before removal in an outpatient setting using local anaesthesia (lidocaine gel) and is retracted via cystoscopy.

TIND 2. Generation: 3-Strut-Nitinol-Implantat

A second-generation TIND device, known as the iTIND, is available and uses only three struts. Its upper section is designed to act on the urethral mucosa, specifically at the bladder neck. This design may help minimise the risk of bladder mucosal injury. [31]. The German AWMF S2k (2023) guideline recommends that TIND can be considered as a treatment alternative for benign prostatic syndrome in prostates with a maximum volume of 75 cm^3 and without an intravesical median lobe, and can be offered particularly to patients who wish to preserve ejaculatory function (level of evidence: expert consensus) [32]. Features of the intervention are provided in Table 1-1.

Table 1-1: Features of the intervention and comparators

	Intervention/Technology	Comparator 1	Comparator 2
Name	Temporary Implantable Nitinol Device (TIND)	Transurethral resection of the prostate (TURP: monopolar or bipolar)	Open prostatectomy or adenomectomy (OP)
Proprietary name	iTIND™ (by Medi-Tate)	NA	NA
Manufacturer	Medi-Tate Ltd. (a subsidiary of Olympus Corporation)	NA	NA
Names in other countries	Known as iTIND in various regions	TURP	Open prostatectomy or adenomectomy (OP)
Device classification	CE marked Class IIa (EU), Class II (FDA)	NA (Surgical procedure)	NA (Surgical procedure)

Abbreviations: EU … European Union; FDA … U.S. Food and drug Administration; NA … Not Applicable; OP … Open Prostatectomy; TURP … Transurethral Resection of the Prostate.

1.2 Summary of previous assessment 2021

Erst-Assessment: keine RCT-Evidenz für TIND

The previous AIHTA assessment [33] was based on the EUnetHTA report OTCA27 [34], which evaluated the comparative effectiveness and safety of multiple surgical techniques and devices for BPH. For TIND, the report found no RCT evidence at the time the report was published.

[12] **A0001** – For which health conditions, and for what purposes, is the technology used?

UPDATE 2025

2 Objectives and scope

Update 2021 EUnetHTA Report mit Fokus auf TIND

This assessment updates a previous AIHTA report that was based on the 2021 EUnetHTA assessment. While maintaining the original population scope, we focused specifically on TIND. To gain comprehensive insights into the intervention's safety profile, we expanded our evidence base to include observational studies, which were not considered in the previous assessment.

2.1 PICO question

PIKO-Frage

In adults with lower urinary tract symptoms, is TIND, in comparison to TURP, OP or adenomectomy in patients with LUTS, more effective and safe concerning International Prostate Symptom Score (IPSS), maximum urinary flow rate (Qmax), post-void residual (PVR), adverse events (AEs) and serious adverse events (SAEs)?

2.2 Inclusion criteria

Einschlusskriterien für relevante Studien

Inclusion criteria for relevant studies are summarised in Table 2-1.

Table 2-1: Inclusion criteria

Population	■ The target condition is lower urinary tract symptoms (LUTS) attributed to non-neurological benign prostatic hyperplasia (BPH) (ICD-9 600.0; ICD-10 N40; MeSH term "Prostatic Hyperplasia"). ■ The target population is adult men (>18 years of age) with LUTS attributed to BPH of non-neurological cause. ■ Either prostate weight or size will be used to define three relevant subpopulations often identified in guidelines (prostate size <30 mL, 30-80 mL and >80 mL. **Rationale:** According to the American Urological Association guidelines [35], men with clinically significant LUTS attributable to BPH who do not find adequate relief with medical treatment or find the side effects of medical treatment bothersome may benefit from surgical treatment. Surgical treatment should be chosen for patients who: ■ did not improve after medical therapy; ■ do not want medical therapy but request active treatment (patient preference); or ■ present with a strong indication for therapy (refractory urinary retention, renal insufficiency due to BPH, bladder stones, recurrent urinary tract infection, recurrent haematuria refractory to 5α-reductase-inhibitors).
Intervention	Temporary implantable nitinol device (TIND) TIND is designed primarily as an alternative to standard care for the treatment of LUTS caused by BPH, particularly for patients seeking a minimally invasive option *MeSH terms: N/A*

Control	■ Transurethral resection of the prostate (TURP: monopolar or bipolar) ■ Open prostatectomy or adenomectomy (OP) *MeSH terms:* transurethral resection of prostate, prostatectomy ■ Rationale: TURP (monopolar or bipolar) is the gold standard surgical treatment for moderate-to-severe BPH-related LUTS and is the most commonly performed procedure worldwide. OP/adenomectomy is the preferred option for very large prostates (>80-100 mL) where TURP may not be effective.
Outcomes	**Effectiveness* (prioritised by critical outcomes):** ■ IPSS 9 (6-9), critical ■ PVR 8 (2-9), critical ■ Qmax 8.5 (2-9), critical ■ Reintervention 7.5 (6-9), critical ■ BPH Impact Index 7 (1-9), critical ■ QoL measures (generic) 6.5 (2-9), critical ■ Persistent irritative symptoms 6.5 (1-9), critical ■ Qmed 4.5 (1-8), important ■ Postoperative LUTS 5.5 (1-9), important **Safety:** adverse events or serious adverse events (e.g. intraoperative complications, postoperative complications) *Scoring was devised by an assessment team using the GRADE approach [1]
Study design	Randomised controlled trials
Efficacy	Randomised controlled trials Prospective non-randomised controlled trials adjusted for confounding variables
Safety	Randomised controlled trials Prospective non-randomised controlled trials Prospective case series with a minimum of 50 participants* *Small studies (e.g. fewer than 50 participants) can have high variability in adverse event rates, making it difficult to distinguish true safety signals from random fluctuations. A sample size of at least 50 provides a more stable estimate of adverse event frequencies, reducing the risk of overinterpreting outliers.

Abbreviations: BPH … benign prostatic hyperplasia; IPSS … International Prostate Symptom Score; LUTS … lower urinary tract symptoms; OP … open prostatectomy; PVR … post-void residual volume; Qmax … maximum urinary flow rate; Qmed … median urinary flow rate; QoL … quality of life; TIND … temporary implantable nitinol device; TURP … transurethral resection of the prostate

3 Methods

3.1 Research questions

Assessment elements from the European Network for Health Technology Assessment (EUnetHTA) Core Model® for the production of Rapid Relative Effectiveness Assessments (Version 4.2) were customised to the specific objectives of this assessment. Please refer to Appendix (Table A-7 to Table A-10) for the detailed research questions.

3.2 Clinical effectiveness and safety

3.2.1 Systematic literature search

systematische Literatursuche in 4 Datenbanken

The systematic literature search was conducted on 17 December 2024 in the following databases:

- Medline via Ovid
- Embase
- Cochrane Library
- CRD (DARE, NHS-EED, HTA)

Suche nach laufenden Studien

The systematic search was limited to the years 2021 to 2024. After deduplication, overall 151 citations were included. The specific search strategy employed can be found in the Appendix.

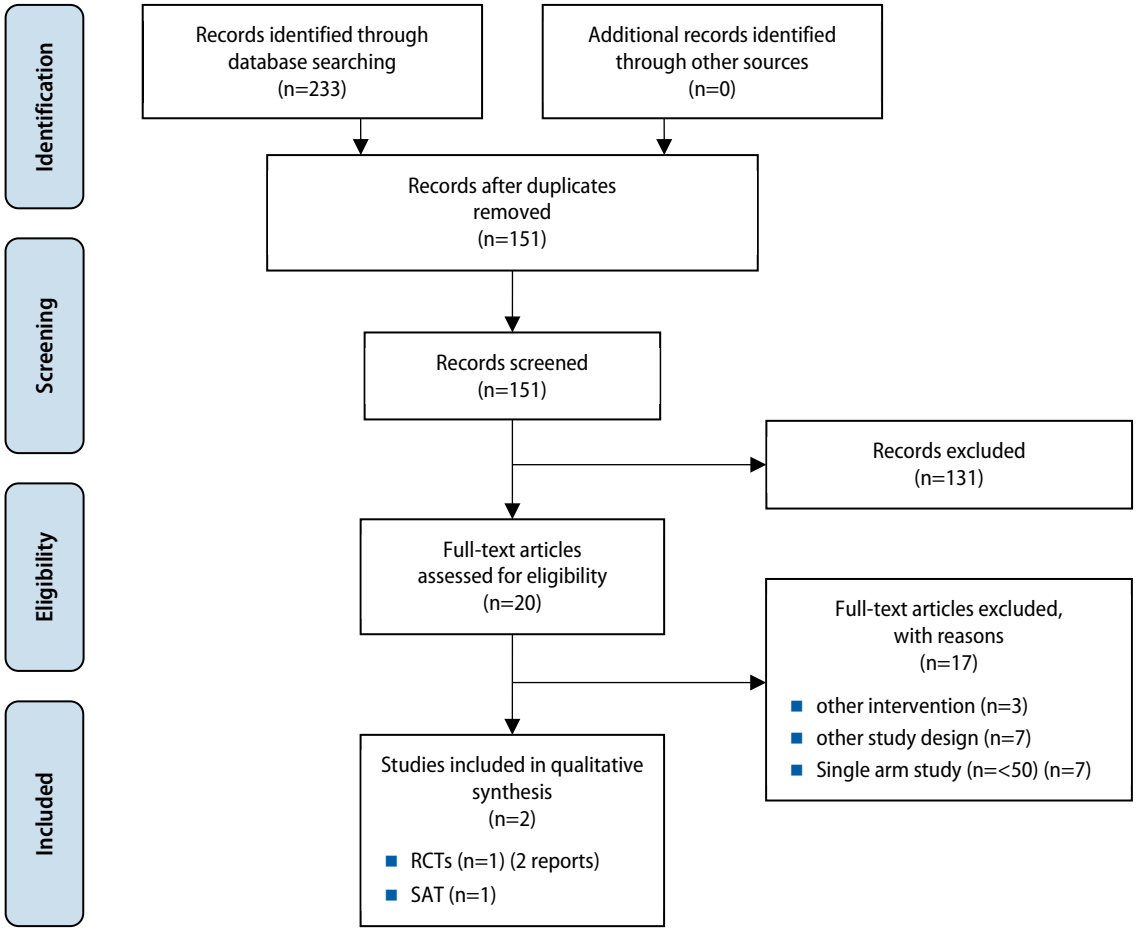
insgesamt 233 Publikationen identifiziert

Furthermore, to identify ongoing and unpublished studies, a search in three clinical trial registries (ClinicalTrials.gov; WHO ICTRP; EU Clinical Trials) was conducted on 13 January 2025, resulting in 20 potentially relevant hits.

3.2.2 Flow chart of study selection

Literaturauswahl

Overall, 233 hits were retrieved, and 151 were identified for screening after deduplication. Two independent researchers screened the references, and in cases of disagreement, a third researcher was involved in resolving the differences. The selection process is displayed in Figure 2-1.



Abbreviations: SAT … single-arm trial; RCT … randomised controlled trial

Figure 2-1: Flow chart of study selection (PRISMA flow diagram)

3.2.3 Analysis

Risk of Bias: Cochrane RoB v.2

Certainty was evaluated using the Cochrane Risk of Bias 2 (RoB2) tool for RCTs. The certainty of the data was assessed using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach.

Single-arm studies were not assessed for RoB as per methodological guidelines and recommendations because they are typically considered lower-quality evidence due to these limitations and are excluded from formal RoB assessments [36]. Single-arm studies with ≥50 participants were included in the safety assessment. Smaller studies can have high variability in adverse event rates, making distinguishing true safety signals from random fluctuations difficult. A minimum sample size of ≥50 helps provide a more stable estimate of adverse event frequencies, reducing the risk of overinterpreting outliers.

4-Augen-Prinzip bei allen Arbeitsschritten

One reviewer (JR or GG) systematically extracted relevant data from the included studies into data extraction tables. A second reviewer (JR or GG) cross-checked the data extraction tables for accuracy. RoB appraisal was conducted in duplicate by two reviewers (JR and GG); differences were settled via consensus. For data extraction and RoB, a third reviewer was called upon to settle any disagreements. One reviewer (JR) analysed the certainty of the data using GRADE, and a second reviewer (GG) validated the analysis.

3.2.4 Synthesis

Zusammenfassung der Ergebnisse mit GRADE

The questions were answered in plain text format with reference to GRADE evidence tables that are included in the Appendix; results were summarised in Table 5-1.

4 Results: Clinical effectiveness and safety

4.1 Outcomes

4.1.1 Outcomes effectiveness

entscheidungsrelevante Endpunkte:

As in the previous assessment scope, the following clinical outcomes were defined as *critical* to derive a recommendation:

IPSS: 7 Fragen zu Harnwegssymptomen

- **International Prostate Symptom Score (IPSS)**
  The IPSS is a standardised questionnaire used to assess the severity of LUTS, primarily in men with BPH. It consists of seven questions evaluating urinary symptoms such as frequency, urgency, weak stream, straining, nocturia, intermittency and incomplete emptying. Each question is scored from 0 to 5, with higher scores being worse. Total scores range from 0 to 35. A 3 points reduction or above is considered minimally clinically important change, and this threshold has been adopted in clinical trials in outcome reporting [37].

PVR: Indikator für Obstruktion/Kontraktilität

- **Post-void residual volume (PVR)**
  The PVR volume is a clinical measure to assess the amount of urine remaining in the bladder after urination. In the context of LUTS in men, PVR is an important indicator for evaluating bladder function and can help identify issues such as bladder outlet obstruction or poor bladder contractility, which are common in conditions like BPH. A higher residual voiding volume indicates a worse outcome. There are no well-established clinical important differences for PVR, as it is an objective measure and patient-perceived benefit is less direct [1].

Qmax: Bewertung von Harnfluss/Obstruktio

- **Maximum urinary flow (Qmax)**
  Qmax is a key urodynamic measure to assess urinary flow efficiency and obstruction. It represents the peak flow rate (mL/s) during voiding and is commonly used in the evaluation of LUTS, particularly in conditions like BPH. A Qmax ≥15 mL/s is generally considered normal, while a Qmax <10 mL/s may indicate significant bladder outlet obstruction. An increase of approximately 2 mL/s in Qmax is often empirically regarded as the MCID for flow rate improvement [1].

Reintervention, BPH Index, Lebensqualität, irritative Symptome

Besides the three critical outcomes above, reintervention, BPH Impact Index, quality of life measures and persistent irritative symptoms were also considered as critical outcomes. It appears these outcomes were not reported in the included studies.

4.1.2 Outcomes safety

und schwerwiegende Nebenwirkungen

As in the previous versions of this report, the following outcomes were defined as *critical* to derive a recommendation:

- Serious adverse events (SAEs) are defined as 'an adverse event (AE) that results in death, is life-threatening, leads to hospitalisation (or prolonged existing hospitalisation), results in persistent or significant disability, a congenital disability, or any other important medical event that may jeopardise the patient or require medical intervention to prevent any of the outcomes listed above'. AEs deemed as serious by the study investigators of each trial have been considered relevant [38].

- Adverse events (AEs), irrespective of severity, are defined as any unanticipated medical incident in a patient who has received a treatment, which does not have to be causally related to the treatment administered [38]. AEs identified and deemed relevant by the study investigators of each trial have been considered relevant.

4.2 Included studies

4.2.1 Included studies effectiveness

Study and population characteristics

Wirksamkeit TIND: 1 RCT, n=185, TIND vs. Sham

Sicherheit TIND: Zusätzliche einarmige Beobachtungsstudie

One RCT evaluated the effectiveness of TIND in adult males with LUTS, while a separate single-arm study was included for the safety analysis. The RCT compared TIND to a sham procedure in 185 participants with a mean age of 61. This multisite trial was conducted in the United States and Canada. The inclusion criteria stipulated subjects are aged 50 years or older. They must be male with symptomatic BPH, an IPSS of ≥10, peak urinary flow rate (PFR) of ≤12 mL/sec with a 125 mL voided volume, prostate volume between 25 and 75 cc, and normal urinalysis. Subjects were excluded if they had cardiac arrhythmias, cardiac disease (including congestive heart failure), uncontrolled diabetes mellitus, significant respiratory disease or known immunosuppression. Those with neurogenic bladder or sphincter abnormalities due to Parkinson's disease, multiple sclerosis, stroke or diabetes were excluded. Also, subjects with a PVR volume greater than 250 mL, as measured by ultrasound, or a history of acute urinary retention, compromised renal function, defined as a serum creatinine level greater than 1.8 mg/dl were excluded.

Sham-Kontrollgruppe: 18F Foley-Katheter

The TIND device is comprised of three elongated, intertwined nitinol struts at the 12, 5 and 7 o'clock positions, an anti-migration anchoring leaflet at 6 o'clock, and a polyester retrieval suture for easy device removal. The sham control arm received the insertion and removal of an 18F silicon Foley catheter in order to simulate both the implantation and retrieval procedures of TIND. The RCT was sponsored by Medi-Tate Ltd.

primäre Ergebnisse: 3 Monate (verblindet)

Primary results were reported at three months (blinded). Participants were unblinded at three months and followed up for 12 months. Loss to follow-up was 29% in TIND participants and 30% in the sham group.

einarmige Studie: n=81

The single-arm multicentre study included 81 men (median age 65) with LUTS due to BPH. All participants received TIND and were followed for one year. The inclusion criteria stipulated an IPSS of ≥10, maximum urinary flow rate (Qmax) ≤12 mL/s, and prostate volume < 75 mL. Ten patients (12.3%) were lost to follow-up.

Study characteristics and results of included studies are displayed in Table A-1 and Table A-2.

4.3 Results

Function[13]

One RCT [39] reported function outcomes. At three months, the effectiveness of TIND was assessed based on the proportion of patients achieving an IPSS reduction of ≥3 points. This threshold was met by 78.6% of patients in the TIND group, compared to 60% in the sham group, resulting in a difference of 18.6% (P=0.029). At three months, the mean difference in Qmax scores was 2.15 (confidence interval [CI] 0.38 to 3.92), significantly favouring TIND compared to sham. At three months, the mean difference in PVR scores was −7.46 (95% CI −26.98 to 12.06), significantly favouring TIND compared to sham. At three months, the mean difference in SHIM score was 3.02 (95% CI −4.04 to 10.08), with no significant difference between TIND and sham. At three months, the mean difference in IIEF scores was not significantly different between TIND and sham 3.02 (95% CI −4.04 to 10.08).

IPSS-Reduktion ≥3 Punkte: 78,6 % (TIND) vs. 60 % (Sham), stat. signifikant

Health-related quality of life[14]

One RCT [39] reported health-related quality of life (HRQoL) outcomes. At three months, the IPSS quality-of-life (QoL) score was 2.7 ± 1.8 in the TIND group and 3.4 ± 2.0 in the sham group. The difference was not statistically significant (P=.264).

BPH Impact Index is also considered as critical functional outcomes. However, the two outcomes were not reported by the RCT.

Lebensqualität: keine stat. signifikanten Unterschiede

Patient satisfaction[15]

No evidence was found to answer the research question.

Patientenzufriedenheit: keine Evidenz

Patient safety[16,17,18]

One RCT [39] reported patient safety data. The total number of adverse events recorded in the TIND group was 109 from 45 participants. The sham group recorded 19 events from 10 participants. The number of participants experiencing ≥1 AE within 30 days was 45 participants (38%) in the TIND group versus 10 participants (18%) in the sham arm. One RCT [39] reported mortality, with one death in the TIND arm (1/128) and no deaths in the sham arm. The cause of death was not reported.

Unerwünschte Ereignisse (UE): 109 (TIND) vs. 19 (Sham)

Serious adverse events in the TIND group were 16 events from 10 participants (7.8%) and two events from two participants (3.5%) in the sham group.

Schwerwiegende UE: 7,8 % vs. 3,5 %

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[13] **D0011** – What is the effect of the technology on patients' body functions?

[14] **D0012** – What is the effect of the technology on generic health-related quality of life?

[15] **D0017** – Was the use of the technology worthwhile?

[16] **C0008** – How safe is the technology in comparison to the comparator(s)?

[17] **C0004** – How does the frequency or severity of harms change over time or in different settings? No evidence was found to answer the research question.

[18] **D0003** – What is the effect of the technology on the mortality due to causes other than the target disease?

Weitere UE: höhere Rate in der TIND-Gruppe

Other adverse events included: Dysuria was reported in 27 participants (22.9%) in the TIND group compared to five participants (8.8%) in the sham group. Haematuria was reported in 16 participants (13.6%) in the TIND group, with no reported cases in the sham group. Micturition urgency was reported in six participants (5.1%) in the TIND group, compared to one participant (1.8%) in the sham group. Pollakiuria was reported in eight participants (6.8%) in the TIND group versus one participant (1.8%) in the sham group. Urinary retention was reported in seven participants (5.9%) in the TIND group, with no cases reported in the sham group. Urinary tract infection (UTI) was reported in two participants (1.7%) in the TIND group, with no cases in the sham group. Sepsis was reported in one participant (0.8%) in the TIND group, with no cases in the sham group. Pain was reported in one participant (0.8%) in the TIND group, with no cases in the sham group.

The reader is referred to Table A-1 for further details on the types of AEs reported.

Adverse events (single-arm study)[19]

häufige UE: unter anderem Hämaturie und Miktionsdrang

One study reported safety data for TIND [40]. Haematuria was reported in 12.3% (n=10) of participants, while 11.1% (n=9) experienced micturition urgency. Pain and urinary retention were each observed in 9.9% (n=8) of participants, and 7.4% (n=6) reported dysuria. Urinary tract infections (UTIs) occurred in 6.2% (n=5) of cases, while an increase in voiding symptoms was noted in 1.2% (n=1) of participants. The treatment failure rate was four out of 81 (5%).

The reader is referred to Table A-2 for further details on the types of AEs reported.

Other critical outcomes including reintervention and persistent irritative symptoms were not reported by the RCT. Therefore, no clinical data can be extracted and reported for the three critical outcomes specified in the PICO.

[19] C0008 – How safe is the technology in comparison to the comparator(s)?

5 Certainty of evidence

RoB mit Cochrane RoB v.2

The risk of bias for individual outcomes of the included RCT was assessed with the Cochrane Risk of Bias 2 tool [41] and is presented in Table A-1 in the Appendix.

Vertrauenswürdigkeit der Evidenz nach GRADE

The certainty of evidence was rated according to the GRADE scheme [42] for each endpoint individually. Two independent researchers rated each study. In cases of disagreement, a third researcher was involved to resolve the difference. A more detailed list of criteria applied can be found in the recommendations of the GRADE Working Group [42].

GRADE bestehend aus 4 Kategorien: sehr niedrig bis hoch

GRADE uses four categories to rank the strength of evidence:

- **High** = We are very confident that the true effect lies close to that of the estimate of the effect.
- **Moderate** = 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** = Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
- **Very low** = Evidence either is unavailable or does not permit a conclusion.

Zusammenfassung in Appendix

The ranking according to the GRADE scheme for the research question can be found in the summary of findings table below and in the evidence pro-file in Appendix Table A-6.

Vertrauenswürdigkeit der Evidenz: sehr niedrig

Overall, the strength of evidence for the effectiveness and safety of TIND in comparison to sham is very low.

Table 5-1: Summary of findings table of TIND vs sham

Outcome	Anticipated absolute effects (95% CI)		Effect size (95% CI)	Number of participants (studies)	Certainty of evidence	Comments
	Risk with sham	Risk with TIND				
IPSS reduction ≥3 points (follow-up: mean 3 months)	781 per 1000	596 per 1000	Relative effect: RR 1.31 (1.04 to 1.65)	185 (1 RCT)	⨁◯◯◯ very low [a,b,c]	78.1% and 59.6% of TIND and sham achieved an IPSS reduction ≥3
PVR (mL) (follow-up: mean 3 months)	NA	NA	Absolute Effect: 7.46 lower (26.98 lower to 12.06 higher)	185 (1 RCT)	⨁◯◯◯ very low [a,b,c]	The PVR for TIND patients was 59.44 ml and for sham was 66.90 ml.
Qmax (follow-up: mean 3 months)	NA	NA	Absolute Effect: 2.15 higher (0.38 higher to 3.92 higher)	185 (1 RCT)	⨁◯◯◯ very low [a,b,c]	The Qmax for TIND patients was 13.55 ml/s and for sham was 11.40 ml/s
Serious AE (follow-up: 30 days)]	35 per 1000	85 per 1000	Relative effect: RR 2.42 (0.51 to 11.41)	185 (1 RCT)	⨁◯◯◯ very low [a,b,c]	8.5% and 3.5% of TIND and sham experienced a SAE
Cumulative complicationsd	1900 per 1000	2422 per 1000	Relative effect: RR 1.27 (0.97 to 1.67)	185 (1 RCT)	⨁◯◯◯ very low [a,b,c]	109 complications for every 45 TIND patients and 19 complications for every 10 sham patients

Abbreviations: AE … adverse events; CI … confidence interval; IPSS … International Prostate Symptoms Score; NA … not applicable; RCT … randomised controlled trial; RR … relative risk; SAE … serious adverse event; TIND … temporary implantable nitinol device

Comments:

[a] *Cochrane RoB 2 rated as high overall risk of bias due to high loss to follow-up and no test of success of sham procedure.*

[b] *Comparing TIND to sham introduces serious indirectness because the comparator (sham) is not equivalent to the intended standard of care (transurethral resection of the prostate) or prostatectomy/adenomectomy.*

[c] *While the result is statistically significant (CI does not cross 1), the small sample size (n=185) and the width of the CI suggest uncertainty about the precise effect size. The result comes from only a single study.*

[d] *These numbers reflect the cumulative complications rather than the incidence of patients experiencing at least one complication.*

Note: other critical outcomes were not either not considered by the RCT or not reported in suitable format to be include in the GRADE table.

6 Discussion

Summary of findings

Evidenz aus 1 RCT und 2 Beobachtungsstudien

This HTA aimed to assess the effectiveness and safety of TIND compared to TURP, either monopolar or bipolar, as well as OP or adenomectomy in adult patients with LUTS. The review included one RCT comparing TIND to sham and one single-arm study evaluating TIND, which provided safety data. The review adopted a systematic approach with a rigorous search strategy, ensuring a comprehensive evaluation of the available evidence. The inclusion of an independent review process by two researchers enhances confidence that the selected studies accurately reflect the current body of research on TIND. By employing a structured methodology, this review aimed to provide an objective assessment of the safety and efficacy of TIND in the management of LUTS secondary to BPH.

RCT: TIND zeigt bessere IPSS-Reduktion und Qmax als Scheinverfahren

The RCT reported functional outcomes at three months, with 78.6% of TIND patients and 60% of the sham arm experiencing an IPSS reduction of ≥3 points. While the IPSS reduction in both arms achieved the MCID of 3 points above to have meaningful clinical improvement, the TIND group has achieved statistically significant better IPSS reduction compared to the sham arm. Other measures of function included the mean Qmax and PVR, which significantly favoured TIND. SHIM and IIEF scores were not significantly different between TIND and sham. The IPSS QoL scores were not significantly different between TIND and sham.

Sicherheit: mehr unerwünschte Ereignisse in TIND-Gruppe (38 %) als bei Scheinverfahren (18 %)

The higher incidence of adverse events ≥1 within 30 day in the TIND group (38%) compared to the sham group (18%) raises concerns regarding its safety profile. While many of these adverse events were mild to moderate in severity, the increased frequency of dysuria, haematuria and urinary retention suggests that TIND may not be as well tolerated as initially expected. The single-arm study further supported this trend, reporting a high occurrence of adverse events, though the absence of a control group limits the ability to attribute these effects solely to the device itself.

Update des EUnetHTA-Assessments mit neuem RCT

This systematic review represents the first comprehensive analysis examining TIND's comparative effectiveness and safety profile. No other reviews were identified. Previous systematic reviews, including the 2021 EUnetHTA assessment [1], have evaluated multiple interventions for this indication and conducted network meta-analyses. However, these broader assessments do not incorporate the most recent randomised controlled trial evidence and offer limited insights into TIND's specific comparative effectiveness and safety outcomes.

Evidence gaps and ongoing clinical trials

Limitations of evidence

interne Validität limitiert: kein direkter Vergleich mit Standardtherapie, kurze Nachbeobachtungszeit

The internal validity of the current evidence is limited by the absence of direct head-to-head comparisons between TIND and established surgical treatments such as TURP or open prostatectomy. Although the primary RCT employed a sham control to manage placebo effects, this design does not clarify how TIND compares with well-established interventions. The lack of direct comparison between TIND and established surgical treatment implies there are substantial differences between TIND and its designated comparators.

Therefore, the sham procedure for TIND might be the appropriate comparator. Moreover, the short follow-up period – primarily three months – provides only preliminary insights into efficacy and safety. These factors reduce confidence in the durability of treatment effects and hinder a comprehensive evaluation of late-onset complications.

externe Validität: enge Einschlusskriterien, Beschränkung auf kleinere Prostatavolumina

External validity is constrained by narrow eligibility criteria and limited stratification. Participants in the RCT had prostate sizes of 25-75 ml, while the single-arm study included men with prostates smaller than 75 ml. Without stratification by prostate volume, it remains uncertain whether the findings extend to men with larger prostates. Consequently, the generalisability of current outcomes to broader clinical populations is uncertain. Additional robust and longer-term RCTs, including directc comparisons with standard and minimally invasive surgical therapies, are necessary to establish the broader applicability of TIND. A centralised registry could further support these efforts by facilitating real-world data collection and ongoing safety monitoring.

Ongoing randomised controlled trials

3 laufende RCTs: TIND vs. Scheinverfahren, TIND vs. UroLift und TIND vs. Rezūm

Clinical trial registries were searched to investigate current ongoing clinical trials and address possible gaps in the evidence base. Three ongoing RCTs on the use of TIND were identified in patients with BPH. One trial investigated the use of TIND compared to sham, primarily focusing on safety outcomes. The second trial compares TIND to UroLift, focusing on the incidence of all intraoperative and postoperative complications. The third trial compares TIND to Rezūm, with the primary outcome focusing on the IPSS scale.

Limitations

Limitationen: Sprachbeschränkung, keine Suche nach grauer Literatur

A comprehensive search of medical literature databases was undertaken; however, an extensive grey literature search was not conducted, potentially limiting the identification of unpublished data. Restricting searches to English and German may also have excluded relevant non-English studies. Nevertheless, clinical trial databases were searched, references of retrieved studies (including systematic and narrative reviews) were hand-searched, and some device manufacturers were contacted, reducing the likelihood that major studies were missed. Due to the scope of the project, quantitative synthesis methodologies, such as meta-analysis and indirect comparisons, could not be undertaken to enhance the validity of the clinical data. These are all considered as limitations of the current review.

Diskussion: TIND minimalinvasiv, Vergleich auch zwischen minimal invasiven Verfahren zentral

While the comparison between TIND and other surgical procedures was the intention of this review according to the PICO, it should be noted that TIND, as a minimally invasive procedure, may have significant different safety and effectiveness profiles compared currently established clinical standard of care such as TURP, EEP or OP. RCTs comparing different minimally invasive treatments may become increasingly relevant in future. On the other hand, comparing TIND with medical therapies also has its limitations due to the difference in treatment goals where pharmacological options are focused on symptom management. It is understood that the comparative evidence between TIND and equivalent minimum invasive procedures are still emerging.

Conclusions

keine belastbaren Aussagen zur komparativen Effektivität möglich

One RCT with a small sample size assessed the safety and effectiveness of TIND compared to a sham procedure in patients with LUTS. However, the evidence is of very low certainty, with limited comparative efficacy data reported and short-term follow-up providing no clear long-term evidence on the safety or efficacy of TIND. Adverse events were more frequent in the TIND group than in the sham group. The single-arm TIND study reported a higher incidence of adverse events than the RCT. Based on the best available evidence, TIND is unlikely to significantly change how patients are managed, and the standard of care is still considered the mainstay.

7 Evidence-based conclusions

In Table 7-1 the scheme for evidence-based conclusion is displayed and the according choice is highlighted.

Table 7-1: Evidence-based conclusions

	1	Strong evidence for added benefit in routine use
	2a	Evidence indicates added benefit only in specific indications
	2b	Less robust evidence indicating an added benefit in routine use or in specific indications
X	3	**No evidence or inconclusive evidence available to demonstrate an added benefit of the intervention of interest**
	4	Strong evidence indicates that intervention is ineffective and or harmful

Reasoning:

The current evidence is insufficient to prove that the assessed technology TIND is more effective and safer as standard care. Additional future RCT data may provide clearer insights.

Evidenz unzureichend

Ongoing clinical trials primarily compare TIND to UroLift and Rezūm rather than the established treatments. As a result, re-evaluation is not currently recommended.

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Appendix

Evidence tables of individual studies included for clinical effectiveness and safety

Table A-1: TIND: Results from randomised controlled trials

Author, year	**Chughtai 2021[39],[43]**
NCT	**NCT04760483**
Country	USA & Canada
Sponsor	Medi-Tate Ltd
Intervention/product	TIND
Comparator	Sham
Study design	RCT
Number of pts	185
Inclusion criteria	Men ≥50 years, IPSS of ≥10, PFR of ≤12 mL/sec with a 125 mL voided volume, prostate volume between 25 and 75 cc, and normal urinalysis
Exclusion criteria	Previous prostate surgery, prostate or bladder cancer, neurogenic bladder and/or sphincter abnormalities, or confounding bladder pathologies
Age of patients (yrs)	61.1 (SD 6.%)
Follow-up (months)	3 months (blinded); 3-12 months (unblinded)
Loss to follow-up, n (%) at 3 months	n=34, (29%) TIND; n=17, (30%) sham
Outcomes	
Efficacy	
Disease-specific survival, n (%)	NR
Recurrence, n (%)	NR
Reduction of ≥3 points in IPSS (analysis NR) (at 3 months)	IPSS ≥3 determining the effectiveness of the TIND treatment was achieved at 3 months in 78.6% of TIND patients compared to 60% of sham arm, a difference of 18.6% (P= .029)
IPSS (baseline change score at 3 months) ITT	TIND -9.0 ± 8.5 sham -6.6 ± 9.5 *P*=0.063
IPSS (TIND **baseline change score at 3 months) PP**	TIND -9.48 ± 8.49 (95% CI -11.4 to -7.6) *P*=<0.0001
IPSS QoL (3 months) ITT	TIND 2.7 ±1.8; sham 3.4 ± 2.0 (*P*=0.264)
IPSS QoL (TIND baseline change score at 3 months) PP	-1.96 ± 1.86 (95% CI -2.3 to -1.4) *P*=<.0001
Qmax (TIND baseline change score at 3 months) PP	TIND 5.01 ± 6.39 (95% CI 3.4 to 6.6) *P*=<.0001
Qmax (3 months) (analysis NR) (at 3 months)	TIND 13.55 (SD 6.4) sham 11.4 (SD 5.3)
PVR (mL) (TIND baseline change score at 3 months) PP	TIND -2.20 ± 56.59 (95% CI -16.7 to 12.3) *P*=0.7407
PVR (mL) (3 months) (analysis NR) (at 3 months)	TIND 59.44 (SD 56.43); sham 66.9 (SD 65.1)
SHIM (TIND baseline change score at 3 months) PP (at 3 months) PP	0.40 ± 7.20 (95% CI -1.2 to 2.0) *P*= 0.7078

Author, year	Chughtai 2021[39],[43]
NCT	**NCT04760483**
SHIM (3 months)	TIND 13.7 (SD 7.76) Sham 13.2 (SD 7.9)
IIEF (TIND baseline change score at 3 months) PP	3.83 ± 19.61 (-0.7 to 8.3) *P*= 0.0523
IIEF (3 months)	TIND 43.52 (SD 22.24) Sham 40.5 (SD 22.8)
TIND vs sham Safety	
Overall survival, n (%)	184/185 (99.5%)
Overall complications, n (%) (0-30 days)	109/45 (38.1%) vs 19/10 (17.5%)
Pts with ≥1 AE (0-30 days)	45 (38%) vs 10 (18%)
Serious AE, n (%) (0-30 days)	TIND n=10 (7.8%) Sham n=2 (3.5%)
Minor AE, n (%)	TIND 45/128 (35.16%) Sham 5/57 (8.77%)
Procedure-related AE	NI
Dysuria (0-30 days)	27 (22.9%) vs 5 (8.8%)
Haematuria (0-30 days)	16 (13.6%) vs nil events
Micturition urgency (0-30 days)	6 (5.1%) vs 1 (1.8%)
Pollakiuria (0-30 days)	8 (6.8%) vs 1 (1.8%)
Urinary retention	7 (5.9%) vs nil events (0-30 days) 1 (0.8) (1-3 months)
Urinary tract infection	2 (1.7%) vs nil events (0-30 days) 1 (0.8%) (1-3 months) 1 (0.8%) (3-12 months)
Sepsis/abscess (30 days)	2/128 (1.56%) vs nil events
Pain (30 days)	1 (0.8%) vs nil events
Procedure-related mortality, n (%)	NR
All cause mortality	TIND 1/128 (0.78%) Sham 0/57 (0.00%)

Abbreviations: AE … adverse events; IIEF … International Index of Erectile Function; IPSS … International Prostate Symptoms Score; ITT … intention to treat analysis; TIND … temporary implantable nitinol device; NI … no information; NA … not applicable; NR … not reported; PFR … peak urinary flow rate; PP … per protocol analysis; PVR … post-void residual volume; Qmax … maximum urinary flow rate (in mL/sec); QoL … quality of life; RCT … randomised controlled trial; SD … standard deviation; SHIM … Sexual Health Inventory for Men

Table A-2: TIND: Results from observational studies

Author, year	Porpiglia 2019 [40]
Country	Multinational
Sponsor	NI
Intervention/product	TIND
Comparator	none
Study design	Prospective single-arm trial
Number of pts	81
Inclusion criteria	IPSS ≥10, Qmax ≤12 mL/s, prostate volume <75mL
Age of patients (yrs)	63.9±8.9
Follow-up (months)	1, 3, 6 and 12 months
Loss to follow-up, n (%)	10 (12.3)
Outcomes	
Efficacy	
Safety*	
Overall complications, n (%)	NI
Major AE, n (%)	NI
Minor AE, n (%)	NI
Haematuria	**n=10 (12.3)**
Micturition urgency	**n=9 (11.1)**
Pain	**n=8 (9.9)**
Dysuria	**n=6 (7.4)**
UTI	**n=5 (6.2)**
Urinary retention	**n=8 (9.9)**
Increase in voiding symptoms	**n=1 (1.2)**
Treatment failure rate	**4/81 (5)**
Procedure-related mortality	**NI**

Abbreviations: AE … adverse events; IPSS … International Prostate Symptoms Score; TIND … temporary implantable nitinol device; NI … no information; UTI … urinary tract infection

Note:

** All complications were graded as I or II according to the Clavien-Dindo system and self-limiting, and occurred in the short-term (54.7% ≤7 days; 30.2% 8-20 days; 15.1% 20-30 days)*

Risk-of-bias tables and GRADE evidence profile

Internal validity of the included studies was judged by 2 independent researchers. In cases of disagreement, a third researcher was involved to resolve the differences. A more detailed description of the criteria used to assess the internal validity of the individual study designs can be found in the Internal Manual of the AIHTA [2] and in the Guidelines of EUnetHTA [3].

Table A-3: Risk of bias – outcome level (randomised studies)

Trial	Endpoints	Bias arising from the randomisation process	Bias due to deviations from intended interventions	Bias due to missing outcome data	Bias in measurement of the outcome	Bias in selection of the reported result	Overall risk of bias
Chughtai 2021[39]	PRO: IPSS Endpoint 1	Low[1]	Low[2]	Some concern[3]	Some concerns[4]	High[5]	High
	PRO IPSS QoL Endpoint 2	Low[1]	Low[2]	Some concern[3]	Some concern[6]	High[5]	High
	Qmax	Low[1]	Low[2]	Some concern[3]	Some concern[6]	High[5]	High
	PVR	Low[1]	Low[2]	Some concern[3]	Some concern[6]	High[5]	High
	SAF	Low[1]	Low[2]	Some concerns[3]	Low	Low[7]	High

Abbreviations: IPSS … International Prostate Symptom Score; PRO … patient-reported outcomes; PVR … post-void residual volume; Qmax … maximum urinary flow rate; SAF … safety endpoints

Notes:

[1] *Adequate allocation sequence (random permuted blocks), baseline imbalances in Charlson Comorbidity Index (CCI) present, but not judged as an indication for improper randomisation (13 tests on different baseline characteristics)*

[2] *Single-blinded design, ITT; missing data appropriately handled*

[3] *30% loss to follow-up in both groups; there is no evidence that the result was not biased by missing outcome data, yet we do not know whether it is likely that missingness depended on true value*

[4] *Method of measuring the outcome appropriate; high risk for 12 months results as patients and outcome assessors had knowledge of intervention. No formal test for reliability of the sham procedure was performed, hence patients could have been aware within 3 months follow-up as well.*

[5] *Emphasis on within-group changes when between-group differences were not significant (e.g. IPSS results); lack of consistent reporting of between-group differences, selective reporting of stat. significance*

[6] *Not clearly stated whether technicians performing testing were blinded but less likely that knowledge of intervention influenced assessment as more objective measurement*

[7] *No indication for selective outcome reporting for safety results*

Table A-4: Evidence profile: efficacy and safety of TIND compared to standard of care

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	TIND	Sham	Relative (95% CI)	Absolute (95% CI)		
IPSS reduction ≥3 points (follow-up: mean 3 months)												
1	randomised trials	serious[a]	not serious	serious[b]	serious[c]	none	100/128 (78.1%)	34/57 (59.6%)	**RR 1.31** (1.04 to 1.65)	**185 more per 1,000** (from 24 more to 388 more)[e]	⨁◯◯◯ Very low[a,b,c]	CRITICAL
IPSS QoL (follow-up: mean 3 months)												
1	randomised trials	serious[a]	not serious	serious[b]	serious[c]	none	128	57	-	MD **0.4 higher** (0.3 lower to 1.1 higher)	⨁◯◯◯ Very low[a,b,c]	CRITICAL
Qmax (follow-up: mean 3 months)												
1	randomised trials	serious[a]	not serious	serious[b]	serious[d]	none	128	57	-	**2.15 higher** (0.38 higher to 3.92 higher)	⨁◯◯◯ Very low[a,b,d]	CRITICAL
PVR (mL) (follow-up: mean 3 months)												
1	randomised trials	serious[a]	not serious	serious[b]	serious[d]	none	128	57	-	**7.46 lower** (26.98 lower to 12.06 higher)	⨁◯◯◯ Very low[a,b,d]	CRITICAL
SHIM (follow-up: mean 3 months)												
1	randomised trials	serious[a]	not serious	serious[b]	serious[d]	none	128	57	-	MD **3.02 higher** (4.04 lower to 10.08 higher)	⨁◯◯◯ Very low[a,b,d]	
Serious AE (follow-up: 30 days)												
1	randomised trials	serious[a]	not serious	serious[b]	serious[d]	none	10/118 (8.5%)	2/57 (3.5%)	**RR 2.42** (0.51 to 11.41)	**50 more per 1,000** (from 17 fewer to 365 more)[f]	⨁◯◯◯ Very low[a,b,d]	
Overall complications (follow-up: 30 days)												
1	randomised trials	serious[a]	not serious	serious[b]	serious[d]	none	109	19	**RR 1.27** (0.97 to 1.67)	**513 more per 1,000** (from 57 fewer to 1,000 more)[g]	⨁◯◯◯ Very low[a,b,d]	

Abbreviations: CI … confidence interval; IPSS … International Prostate Symptom Score; MD … mean difference; QoL … quality of life; RR … risk ratio; SHIM … Sexual Health Inventory for Men

Explanations:

[a] *Cochrane RoB 2 rated as high overall risk of bias due to high loss to follow-up and no test of success of sham procedure.*

[b] *Comparing TIND to sham introduces serious indirectness because the comparator (sham) is not equivalent to the intended standard of care (transurethral resection of the prostate) or prostatectomy/adenomectomy.*

[c] *While the result is statistically significant (CI does not cross 1), the small sample size n=185) and the width of the CI suggest uncertainty about the precise effect size. The result comes from only a single study.*

[d] *The small sample size (n=185) and the width of the CI suggest uncertainty about the precise effect size. The result comes from only a single study.*

[e] *Out of every 1,000 men receiving TIND, an estimated 185 more men would experience at least a 3-point improvement in their symptoms compared to those who had the sham procedure. However, the actual number could range from 24 more to 388 more due to uncertainty in the estimate.*

[f] *Out of every 1,000 men receiving TIND, an estimated 50 more serious adverse events occur compared with those who had the sham procedure. However, the actual number could range from 17 fewer to 365 more due to uncertainty in the estimate.*

[g] *Out of every 1,000 men receiving TIND, as estimated 513 more complications occur compared with those who had the sham procedure. However, the actual number could range from 57 fewer to 1,000 more due to uncertainty in the estimate.*

Applicability table

Table A-5: Summary table characterising the applicability of a body of studies

Domain	Description of applicability of evidence
Population	The included study specified that the eligible patients must be over 18 years of age with LUTS attributed to BPH of non-neurological cause. IPSS of ≥10, PFR of ≤12 mL/sec with a 125 mL voided volume, prostate volume between 25 and 75 cc, and normal urinalysis, complete blood count and biochemistry. From the trial, all patients were male with the mean age of 61 years The mean weight approximately 88 kg with the BMI of 28.8. Guidelines define subpopulations based on prostate size: <30 mL, 30-80 mL, and >80 mL. The included RCT investigated patients with prostate size between 25 and 75 mL. This range is across two subpopulations defined by guidelines. The study is not applicable to prostate size >80 mL.
Intervention	TIND a minimally invasive temporary device. The current best practice i.e. TURP (monopolar or bipolar) and open prostatectomy or adenomectomy are not minimally invasive procedures. Therefore there is no applicability concern regarding the intervention.
Comparators	The comparator is sham procedures. No current best practice comparator was identified comparing TIND within RCT settings.
Outcomes	Outcomes were assessed from baseline to 3 months (blinded) and further follow-up data was reported at 12 months in the unblinded TIND arm. Outcomes were reduction of ≥3 points in IPSS, IPSS baseline change scores, IPSS QoL, Qmax (change score), PVR (mL) (change score), SHIM, IIEF, complication, adverse events. There are no applicability concerns.
Setting	TIND procedure was conducted at 16 sites in the USA and Canada. There are no applicability concerns.

Abbreviations: BMI … body mass index; BPH … benign prostatic hyperplasia; IIEF … International Index of Erectile Function; IPSS … International Prostate Symptom Score; LUTS … lower urinary tract symptoms; PFR … ; PVR … post-void residual volume; PSA … prostate-specific antigen; RCT … randomised controlled trial; Qmax … maximum urinary flow rate; QoL … quality of life; TIND … temporary implantable nitinol device; TURP … transurethral resection of the prostate; SD … standard deviation; SHIM … Sexual Health Inventory for Men

List of ongoing randomised controlled trials

Table A-6: List of ongoing randomised controlled trials of TIND

Identifier/ trial name	Patient population	Inclusion criteria	Intervention	Comparison	Primary outcome	N of pts (planned)	Primary completion date	Sponsor
NCT04987138	BPH | LUTS	Adults ≥45 years of age; baseline IPSS score ≥13; ≥1 in the IPSS voiding to storage sub-score ratio (IPSS-V/S) Prostate volume 25-80 cc by TRUS, measured within 120 days post study consent	Zenflow Spring System	Sham	Safety	N=279	30.06.2024	Zenflow, Inc.
NCT04757116	BPH	Males ≥50 years with LUTS due to BPH; IPSS ≥13; Qmax 5-15 mL/sec (voided volume ≥125 mL) and prostate volume ≤75 cc; PSA <4 ng/mL, or 4-10 ng/mL if prostate cancer is ruled out; must provide informed consent and complete all study visits	TIND	UroLift	Incidence of all intraoperative and postoperative complications	206	31.12.2025	Olympus Corporation of the Americas
NCT06275256	BPH	Patients >18 years of age, undergoing Rezūm or TIND treatment	TIND	Rezūm	IPSS	N=20	01.03.2025	University of Manitoba

Abbreviations: BPH … benign prostatic hyperplasia; IPSS … International Prostate Symptom Score; LUTS … lower urinary tract symptoms; N … number; NI … no information; TIND … temporary implantable nitinol device; TRUS … transrectal ultrasound

Research questions

Table A-7: Health problem and current use

Element ID	Research question
A0001	For which health conditions, and for what purposes, is the technology used?
A0002	What is the disease or health condition in the scope of this assessment?
A0003	What are the known risk factors for the disease or health condition?
A0004	What is the natural course of the disease or health condition?
A0005	What is the burden of disease for the patients with the disease or health condition?
A0006	What are the consequences of the disease or health condition for the society?
A0024	How is the disease or health condition currently diagnosed according to published guidelines and in practice?
A0025	How is the disease or health condition currently managed according to published guidelines and in practice?
A0007	What is the target population in this assessment?
A0023	How many people belong to the target population?
A0011	How much are the technologies utilised?

Table A-8: Description of the technology

Element ID	Research question
B0001	What is the technology and the comparator(s)?
A0020	For which indications has the technology received marketing authorisation or CE marking?
B0002	What is the claimed benefit of the technology in relation to the comparator(s)?
B0003	What is the phase of development and implementation of the technology and the comparator(s)?
B0004	Who administers the technology and the comparator(s) and in what context and level of care are they provided?
B0008	What kind of special premises are needed to use the technology and the comparator(s)?
B0009	What supplies are needed to use the technology and the comparator(s)?
A0021	What is the reimbursement status of the technology?

Table A-9: Clinical effectiveness

Element ID	Research question
D0001	What is the expected beneficial effect of the technology on mortality?
D0003	What is the effect of the technology on the mortality due to causes other than the target disease?
D0005	How does the technology affect symptoms and findings (severity, frequency) of the disease or health condition?
D0006	How does the technology affect progression (or recurrence) of the disease or health condition?
D0011	What is the effect of the technology on patients' body functions?
D0016	How does the use of technology affect activities of daily living?
D0012	What is the effect of the technology on generic health-related quality of life?
D0013	What is the effect of the technology on disease-specific quality of life?
D0017	Was the use of the technology worthwhile?

Table A-10: Safety

Element ID	Research question
C0008	How safe is the technology in comparison to the comparator(s)?
C0002	Are the harms related to dosage or frequency of applying the technology?
C0004	How does the frequency or severity of harms change over time or in different settings?
C0005	What are the susceptible patient groups that are more likely to be harmed through the use of the technology?
C0007	Are the technology and comparator(s) associated with user-dependent harms?
B0010	What kind of data/records and/or registry is needed to monitor the use of the technology and the comparator?

Literature search strategies

Search strategy for Cochrane

Search name: TIND (Update)	
Search date: 17 December 2024	
ID	Search
#1	MeSH descriptor: [Prostatic Hyperplasia] explode all trees
#2	(prostat* NEXT hyper?plasia*) (Word variations have been searched)
#3	MeSH descriptor: [Lower Urinary Tract Symptoms] explode all trees
#4	("lower urinary tract" NEXT symptom*) (Word variations have been searched)
#5	MeSH descriptor: [Prostatism] explode all trees
#6	(prostatism*) (Word variations have been searched)
#7	(BPH)
#8	(LUTS)
#9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
#10	(nitinol*) (Word variations have been searched)
#11	("titanium nickel" NEXT alloy*) (Word variations have been searched)
#12	("nickel titanium" NEXT alloy*) (Word variations have been searched)
#13	(TIND*)
#14	(i?TIND*) (Word variations have been searched)
#15	(Medi?Tate*) (Word variations have been searched)
#16	#10 OR #11 OR #12 OR #13 OR #14 OR #15
#17	#9 AND #16
#18	#9 AND #16 with Cochrane Library publication date Between Jan 2021 and Dec 2024
#19	(conference proceeding):pt
#20	(abstract):so
#21	(clinicaltrials OR trialsearch OR ANZCTR OR ensaiosclinicos OR Actrn OR chictr OR cris OR ctri OR registroclinico OR clinicaltrialsregister OR DRKS OR IRCT OR Isrctn OR rctportal OR JapicCTI OR JMACCT OR jRCT OR JPRN OR Nct OR UMIN OR trialregister OR PACTR OR R.B.R.OR REPEC OR SLCTR OR Tcr):so
#22	#19 OR #20 OR #21
#23	#18 NOT #22
Total hits: 7	

Search strategy for Embase

Search name: TIND (Update)		
Search date: 17 December 2024		
No.	Query Results	Results
#1	'prostate hypertrophy'/exp	47,036
#2	'prostat* hyperplasia'	29,483
#3	'prostat* hyper-plasia*'	24
#4	bph	29,178
#5	'lower urinary tract symptom'/exp	21,466
#6	'low* urinary tract symptom*'	27,508
#7	luts	12,864
#8	'prostatism'/exp	1,033
#9	prostatism*	1,451

#10	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9	80,110
#11	'nitinol'/exp	6,262
#12	nitinol*	11,967
#13	'nickel titanium alloy*'	431
#14	'titanium nickel alloy*'	39
#15	'temporary implantable nitinol device'/exp	20
#16	tind	213
#17	'itind'/exp	14
#18	i$tind	87
#19	'i-tind*'	15
#20	'medi-tate*'	39
#21	'medi?tate*'	148
#22	#11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18	12,563
#23	#10 AND #22	208
#24	#23 AND [2021-2024]/py	116
#25	#24 AND 'Conference Abstract'/it	43
#26	#24 NOT #25	73
Total hits: 73		

Search strategy for Medline via Ovid

Search name: TIND (Update)	
Search date: 17 December 2024	
ID	Search
#1	exp Prostatic Hyperplasia/ (25031)
#2	prostat* hyper?plasia*.mp. (31883)
#3	prostat* hyper-plasia*.mp. (5)
#4	exp Lower Urinary Tract Symptoms/ (48205)
#5	lower urinary tract symptom*.mp. (12754)
#6	exp Prostatism/ (562)
#7	prostatism*.mp. (1105)
#8	BPH.mp. (14610)
#9	LUTS.mp. (6147)
#10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 (83413)
#11	nitinol*.mp. (4827)
#12	titanium nickel alloy*.mp. (36)
#13	nickel titanium alloy*.mp. (361)
#14	TIND*.mp. (456)
#15	i?TIND*.mp. (58)
#16	i-TIND*.mp. (5)
#17	Medi-Tate*.mp. (16)
#18	or 12 or 13 or 14 or 15 or 16 or 17 (5593)
#19	10 and 18 (108)
#20	limit 19 to yr="2021 - 2024" (59)
#21	remove duplicates from 20 (59)
Total hits: 59	

Search strategy for HTA-INATHTA

Search name: TIND (Update)	
Search date: 17 December 2024	
ID	Search
#1	"Prostatic Hyperplasia"[mhe]
#2	prostat* hyperplasia*
#3	"Lower Urinary Tract Symptoms"[mhe]
#4	lower urinary tract symptom*
#5	"Prostatism"[mhe]
#6	prostatism*
#7	BPH
#8	LUTS
#9	(LUTS) OR (BPH) OR (prostatism*) OR ("Prostatism"[mhe]) OR (lower urinary tract symptom*) OR ("Lower Urinary Tract Symptoms"[mhe]) OR (prostat* hyperplasia*) OR ("Prostatic Hyperplasia"[mhe])
#10	nitinol*
#11	titanium nickel alloy*
#12	nickel titanium alloy*
#13	TIND*
#14	iTIND*
#15	i-TIND*
#16	Medi-Tate*
#17	MediTate*
#18	(MediTate*) OR (Medi-Tate*) OR (i-TIND*) OR (iTIND*) OR (TIND*) OR (nickel titanium alloy*) OR (titanium nickel alloy*) OR (nitinol*)
#19	((MediTate*) OR (Medi-Tate*) OR (i-TIND*) OR (iTIND*) OR (TIND*) OR (nickel titanium alloy*) OR (titanium nickel alloy*) OR (nitinol*)) AND ((LUTS) OR (BPH) OR (prostatism*) OR ("Prostatism"[mhe]) OR (lower urinary tract symptom*) OR ("Lower Urinary Tract Symptoms"[mhe]) OR (prostat* hyperplasia*) OR ("Prostatic Hyperplasia"[mhe]))
Total hits: 0	

Search strategy for ClinicalTrials.gov

Search name: TIND (Update)	
Search date: 13 January 2025	
ID	Search
#1	Prostatic Hyperplasia OR Prostatic Hypertrophy OR Enlarged Prostate OR BPH OR Lower Urinary Tract Symptoms OR LUTS OR Prostatism *in Condition/disease*
#2	Nitinol OR "titanium nickel alloy" OR "nickel titanium alloy" OR iTIND OR TIND OR Medi-Tate OR MediTate *in Intervention/treatment*
Total hits: 18	

Search strategy for WHO ICTRP

Search name: TIND (Update)	
Search date: 13 January 2025	
ID	Search
#1	Prostatic Hyperplasia OR Prostatic Hypertrophy OR Enlarged Prostate OR BPH OR Lower Urinary Tract Symptoms OR LUTS OR Prostatism *in the Condition*
#2	Nitinol OR "titanium nickel alloy" OR "nickel titanium alloy" OR iTIND OR TIND OR Medi-Tate OR MediTate *in the Intervention*
Total hits: 8 (2 further) studies identified	

Search strategy for EudraCT

Search name: TIND (Update)	
Search date: 13 January 2025	
ID	Search
#1	Nitinol OR "titanium nickel alloy" OR "nickel titanium alloy" OR iTIND OR TIND OR Medi-Tate OR MediTate
Total hits: 1 (no relevant) study identified	

HTA Austria
Austrian Institute for
Health Technology Assessment
GmbH