Technoleg Iechyd Cymru
Health Technology Wales

Topic Exploration Report

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

1. Determine the quantity and quality of evidence available for a technology of interest.
2. Identify any gaps in the evidence/ongoing evidence collection.
3. Inform decisions on topics that warrant fuller assessment by Health Technology Wales.

Topic:	Prostatic urethral temporary implant insertion for lower urinary tract symptoms caused by benign prostatic hyperplasia
Topic exploration report number:	TER250

Introduction and aims

Health Technology Wales researchers searched for evidence on prostatic urethral temporary implant insertion for lower urinary tract symptoms (LUTS) caused by benign prostatic hyperplasia (BPH). The Manufacturer highlighted iTind but other similar devices will also be considered.

LUTS caused by BPH commonly affect men over 50 years. Stromal and epithelial cells increase in number, causing the prostate to increase in size, with large nodules compressing the urethra. Symptoms include hesitancy during micturition, interrupted or decreased urine stream, nocturia, incomplete voiding and urinary retention.

Mild symptoms are usually managed conservatively. Drugs may also be used, such as alpha blockers and 5-alpha-reductase inhibitors. If other treatments have not worked, there are a range of surgical options that may be considered, including transurethral prostatic resection (TURP), which is considered the 'gold standard' when surgery is indicated. Potential complications of surgical procedures include bleeding, infection, urethral strictures, incontinence and sexual dysfunction.

Prostatic urethral temporary implant insertion aims to relieve symptoms of BPH by creating new channels in the urethra that increase the flow of urine, without having the complications of an implant left in situ. Using local anaesthesia or light sedation, a folded device made from nitinol is inserted into the prostatic urethra with a cystoscope under direct visualisation. The device opens in the prostatic urethra. Over the following days, the pressure applied by struts in the device creates areas of ischaemia in the prostatic urethra and bladder neck. This makes new longitudinal channels through which urine can flow. After five to seven days, lidocaine gel and a flexible silicone extraction catheter are inserted into the urethra and the device is removed. The insertion and removal of the device are performed as day case procedures.

Summary of evidence

UK guidance

National Institute for Health and Care Excellence (NICE) clinical guideline (CG97) recommends that minimally invasive treatments should not be offered as an alternative to surgery (TURP, transurethral vaporisation of the prostate or holmium laser enucleation of the prostate) for managing voiding LUTS presumed secondary to benign prostate enlargement.

NICE interventional procedures guidance (IPG641) recommended that prostatic urethral temporary implant insertion for LUTS caused by BPH should only be used in the context of research as current evidence on the safety and efficacy is limited. This guidance is due to be reviewed in January 2022. IPG641 recommends that further research, ideally in the form of randomised controlled trials (RCTs), should report details of patient selection (including prostate size and the amount of median lobe enlargement), improvement in lower urinary tract symptoms in the short and long term, re-intervention rates, and sexual function outcome measures.

International guidance

While European Association of Urology guidelines acknowledge the emerging role of iTind, no specific recommendations were made (Gravas et al, 2017).

In 2019, the U.S. Food and Drug Administration approved iTind for the treatment of symptoms due to urinary outflow obstruction secondary to BPH in men aged 50 years and above.

Systematic reviews

We identified one systematic reviews investigating minimally invasive procedures for the treatment of LUTS caused by BPH. Tzeng et al (2021) compared prostatic urethral lift, water vapour thermal therapy, and temporary implantable nitinol devices. The temporary implantable nitinol device studies reported varying rates of retreatment and complications. All of the technologies were found to offer low rates of erectile and ejaculatory dysfunction, although the risk appeared to be highest for water vapour thermal therapy.

Primary evidence

In addition to the studies evaluated in the systematic review described above, we identified a number of relevant primary studies.

In one RCT across 16 sites in the USA and Canada, 175 men aged 50 years or older received iTind or sham. Patients were assessed at baseline, 1.5, 3 and 12 months post-operatively. At 3 months, 78.6% of patients in the iTind arm showed a reduction of $\geq$3 points in International Prostate Symptom Score (IPSS), versus 60% of patients in the control arm. At 12 months, the iTind group reported a 9.25 decrease in IPSS ($p<0.0001$), a 3.52 millilitre per second increase in peak flow rate ($p<0.0001$) and a 1.9-point reduction in quality of life ($p<0.0001$) (Chughtai et al, 2020).

In a single-arm, international prospective study (including the UK), Porpiglia et al (2018) evaluated men with BPH-related LUTS who were treated with iTind and followed for one year. In comparison to baseline, none of the 61 patients who completed the 12 month follow-up reported sexual or ejaculatory dysfunction, and all complications graded as $\leq$ 2 Clavien-Dindo were self-limiting. Significant improvements were recorded in IPSS score, quality of life, peak urinary flow rate and post-void residual from baseline to 1 year follow-up. The treatment failure rate was 5%, two patients required TURP, and two patients required

medication. Two year outcomes were reported by Kadner et al (2020), where a significant reduction in symptoms and an improvement in urinary flow were maintained. No deterioration in sexual or ejaculatory function was recorded, and five patients underwent surgery due to treatment failure.

Safety
Adverse events reported in studies investigating prostatic urethral temporary implant insertion for LUTS caused by BPH were typically mild and transient. No de novo ejaculatory or erectile dysfunction occurred.

Cost
We identified one conference abstract (Elterman, 2017) comparing iTind to the prostatic urethral lift system after three years in 32 men. In Canada, the iTind device cost is approximately $2,500 CAD and one device is used per case. The approximate cost of a prostatic urethral lift implant is $800 CAD/implant and the mean number of PUL implants used in the one study was 5.2. Thus, in Canada, the approximate cost per prostatic urethral lift procedure was calculated as $4,160 CAD.

The Manufacturer states that the cost of using iTind is £1,207.50 (excluding VAT) per patient. This cost includes the cost of the device itself as well as the cost of a removal snare and Foley Catheter, which are used in the removal of the iTind device.

Ongoing studies
Health Technology Wales researchers identified three ongoing systematic reviews and a number of primary studies. Details of these can be found in the 'Brief literature search results' section.

Areas of uncertainty

Most of the evidence we identified consisted of single-arm studies, with very few direct comparative clinical trials among minimally invasive BPH technologies or surgical interventions such as TURP. In addition, the studies that were reported tended to have small numbers of participants. There appears to be a lack of long-term data available for prostatic urethral temporary implant insertion for LUTS caused by BPH, with uncertainty around its efficacy in patients with previous prostate cancer, prominent median lobe, large prostate volume, urethral stricture, concomitant bladder stones or previous prostate surgery. The only evidence we identified for cost effectiveness of this technology comes from a conference abstract.

Conclusions

Since the recommendations in NICE IPG641 (2019), a few studies have been published investigating prostatic urethral temporary implant insertion for LUTS caused by BPH. The studies have suggested that this minimally invasive procedure could potentially improve LUTS in some men, particularly in those who are unfit for surgery or those who want to avoid sexual side-effects associated with medical therapy or standard BPH surgery. However, the majority of these studies have not been RCTs, have not reported comparative data, and have not included all types of patients with BPH. Some of the studies published since NICE IPG641 have reported three-year follow-up data, but narrative reviews on the subject suggest that longer

follow-up studies would be beneficial. Evidence for the cost effectiveness of this technology is limited.

Brief literature search results

Resource	Results
HTA organisations	
Healthcare Improvement Scotland	We did not identify any relevant information or guidance from this source.
Health Technology Assessment Group	We did not identify any relevant information or guidance from this source.
Health Information and Quality Authority	We did not identify any relevant information or guidance from this source.
EUnetHTA	We did not identify any relevant information or guidance from this source.
International HTA Database	We did not identify any relevant information or guidance from this source.
U.S. Food and Drug Administration	The iTind System for the treatment of symptoms due to urinary outflow obstruction secondary to benign prostatic hyperplasia (BPH) in men age 50 and above (2019): https://www.accessdata.fda.gov/cdrh_docs/pdf19/DEN190020.pdf
European Society of Urology	Gravas S, Cornu N, Drake MJ, et al. EAU guidelines on non-neurogenic male lower urinary tract symptoms (LUTS), including benign prostatic obstruction (BPO). European Association of Urology, 2017, pp.129–146. DOI: 10.1016/j.eururo.2014.12.038
UK guidelines and guidance	
SIGN	We did not identify any relevant information or guidance from this source.
NICE	CG97. Lower urinary tract symptoms in men: management (updated June 2015): https://www.nice.org.uk/guidance/cg97 IPG641. Prostatic urethral temporary implant insertion for lower urinary tract symptoms caused by benign prostatic hyperplasia (2019): https://www.nice.org.uk/guidance/ipg641
Secondary literature and economic evaluations	
Cochrane library	We did not identify any relevant secondary literature or economic evaluations from this source.
Medline	Tzeng M, Basourakos SP, Lewicki PJ, Hu JC, Le RK (2021). New Endoscopic In-office Surgical Therapies for Benign Prostatic Hyperplasia: A Systematic Review. European Urology Focus: https://doi.org/10.1016/j.euf.2021.02.013
Primary studies	
https://www.epistemonikos.org/en/	We did not identify any relevant information or guidance from this source.
https://www.tripdatabase.com/	did not identify any relevant information or guidance from this source
Cochrane library	Elterman DS (2017). The temporary implantable nitinol device (iTind) for the minimally invasive treatment of benign prostatic hyperplasia: comparison of three-year outcomes and cost in Canada. Canadian urological association journal. Conference: 72nd annual meeting of the canadian urological association. Canada, 11(6 Supplement 4), S228: https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01406544/full?highlightAbstract=iTind
Medline	Kadner G, Valerio M, Giannakis I, Manit A, Lumen N, Ho BSH, Alonso S, Schulman C, Barber N, Amparore D, Porpiglia F (2020). Second generation of temporary implantable nitinol device (iTind) in men with LUTS: 2 year results of the MT-02-study. World Journal of Urology, 38, 3235–3244: https://doi.org/10.1007/s00345-020-03140-z

	Porpiglia F, Fiori C, Amparore D, Kadner G, Manit A, Valerio M, Nicolaas L, Ho BSH, Alonso S, Schulman C (2019) Second-generation of temporary implantable nitinol device for the relief of lower urinary tract symptoms due to benign prostatic hyperplasia: results of a prospective, multicentre study at 1 year of follow-up. BJUI,123(6):1061–1069: https://doi.org/10.1111/bju.14608 Suarez-Ibarrola R, Miernik A, Gratzke C, Schoeb DS (2020). Reasons for new MIS. Let's be fair: iTind, Urolift and Rezūm. World Journal of Urology: https://link.springer.com/article/10.1007/s00345-020-03453-z
Ongoing primary or secondary research	
PROSPERO database	Alexander Light, Dost Jabarkhyl, Oussama Elhage, Prokar Dasgupta. Sexual function following surgery for benign prostatic hyperplasia: a systematic review and network meta-analysis of randomised-controlled trials. PROSPERO 2019 CRD42019155506. Estimated completion date: May 2020 https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019155506 Angela Pecoraro, Enrico Checcucci, Sabrina De Cillis, Daniele Amparore, Federico Piramide, Gabriele Volpi, Giovanni Cacciamani, Cristian Fiori, Francesco Porpiglia, Michele Sica, Stefano Piscitello, Beatrice Carbonaro, Davide Zamengo, Juliette Meziere. NEW ULTRA-MINIMAL INVASIVE SURGICAL TREATMENT FOR BENIGN PROSTATIC HYPERPLASIA: A SYSTEMATIC REVIEW AND POOLED ANALYSIS. PROSPERO 2021. CRD42021225014. Anticipated completion date: January 2021: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021225014 Francesco Cantiello. MECHANICAL AND ABLATIVE MINIMALLY INVASIVE TECHNIQUES FOR MALE LOWER URINARY TRACT SYMPTOMS DUE TO BENIGN PROSTATIC HYPERPLASIA: AN UPDATE OVERVIEW. PROSPERO 2020 CRD42020173409. Anticipated completion date: June 2020 https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020173409
Clinicaltrials.gov	NCT04757116. A Randomized, International Study to Assess the Safety of iTind Compared to TURP (MT-08) 140 participants. Primary outcome: Rate of Adverse events Clavien Dindo grade II or higher. Estimated study completion date: September 2023: https://clinicaltrials.gov/ct2/show/NCT04757116 NCT03395522. Study to Assess the Efficacy of the iTind in Subjects With Symptomatic BPH (MT-06). The study's primary objective is to assess the efficacy of the Medi-Tate iTind in subjects with symptomatic BPH by reduction of International Prostate Symptoms Score) score. 200 participants in single-arm study. Estimated completion date: October 2021: https://clinicaltrials.gov/ct2/show/NCT03395522 NCT03994263. A Prospective Study to Observe the Mechanism of Action of the MediTate iTind in Subjects With Symptomatic BPH With MRI. Active, not recruiting. A total of up to 15 eligible subjects will be enrolled into this open-labeled one-arm study designed to observe the mechanism of action of iTind when using MRI. Estimated completion date: February 2021: https://clinicaltrials.gov/ct2/show/NCT03994263
Other	

Provided by the topic proposer through HealthTech Connect	Chughtai B, Elterman D, Shore N, Gittleman M, Motola J, Pike S, Hermann C, Terrens W, Kohan A, Gonzalez RR, Katz A, Schiff J, Goldfischer E, Grunberger I, Tu LM, Alshak MN, Kaminetzky J (2020). The iTind Temporarily Implanted Nitinol Device for the Treatment of Lower Urinary Tract Symptoms Secondary to Benign Prostatic Hyperplasia: A Multicenter, Randomized, Controlled Trial. Urology: https://doi.org/10.1016/j.urology.2020.12.022

Date of search:	April 2021
Concepts used:	Nitinol device, lower urinary tract symptoms (LUTS), benign prostatic hyperplasia (BPH), TIND, urethral implantable device, prostatic urethral temporary implant insertion