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Medical technology consultation: UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia

Supporting documentation – Committee papers

The enclosed documents were considered by the NICE medical technologies advisory committee (MTAC) when making their draft recommendations:

1. **Original EAC assessment report** – an independent report produced by an external assessment centre who have reviewed and critiqued the available evidence.

2. **EAC assessment report update**– an independent report produced by an external assessment centre who have reviewed and critiqued the available evidence.
3. **EAC assessment report update additional analysis**
4. **Assessment report overview update** – an overview produced by the NICE technical lead which highlights the key issues and uncertainties in the company's submission and assessment report.
5. **Scope of evaluation** – the framework for assessing the technology, taking into account how it works, its comparator(s), the relevant patient population(s), and its effect on clinical and system outcomes. The scope is based on the sponsor's case for adoption.
6. **Review Decision** - documentation detailing the decision to schedule a standard update of the guidance and bring the topic to committee to review new evidence.
7. **Sponsor submission of evidence** – the evidence submitted to NICE by the notifying company.
8. **Expert questionnaires** – expert commentary gathered by the NICE team on the technology.
9. **Company fact check comments** – the manufacturer's response following a factual accuracy check of the assessment report.

Please use the above links and bookmarks included in this PDF file to navigate to each of the above documents.

Cedar

Healthcare Technology Research Centre

External assessment centre report:

The Urolift system for the treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia

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Date: 19/03/15

Version: 2.0

In Version 2 corrections were made to the original version (dated 13/2/2015). This involved changes to the figures in table 60 and to references to them in the text.

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External Assessment Centre report

The purpose of the External Assessment Centre (EAC) report is to review and critically evaluate the sponsor's clinical and economic evidence and may include additional analysis of the submitted evidence or new clinical and/or economic evidence.

Title: The Urolift system for the treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia

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Declared interests of the authors

Description of any pecuniary relationship with sponsors, both personal and of the EAC. Please refer to NICE's Code of Practice for declaring and dealing with conflicts of interests.
http://www.nice.org.uk/niceMedia/pdf/Guidanceondeclarationsofinterest.pdf

Grace Carolan-Rees is employed by the NHS; the NHS has a financial interest in the guidance issued by NICE as a result of this work.

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Dr Antony Wilkes (Statistical consultant, Cedar)

Rider on responsibility for report

The views expressed in this report are those of the authors and not those of NICE. Any errors are the responsibility of the authors.

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1 Summary

Scope of the sponsor's submission

The sponsor's submission contained all published evidence available on the Urolift device, which comprised of uncontrolled before and after studies, or reports of a single sham-controlled, blinded RCT. The completeness of the sponsor's evidence submission was confirmed by an independent EAC literature search. However, the NICE scope called for evidence that included TURP or HoLEP as a comparator and this evidence does not currently exist.

Summary of clinical evidence submitted by the sponsor

The sponsor submitted a peer-reviewed systematic review by Perera et al. (2014) in place of a de novo evidence submission and synthesis. The meta-analysis within Perera et al. (2014) utilizes data from 10 studies on IPSS score, men's sexual health scores, health-related quality of life, urinary flow rate and post-void residual volume. Of the studies used in the systematic review, there were 2 published papers (McVary et al., 2014 & Roehrborn et al., 2013) on a blinded, sham controlled RCT (LIFT Study), and 8 uncontrolled before and after studies (Abad et al., 2013; Cantwell et al., 2014; Chin et al., 2012; Delongchamps et al., 2012; McNicholas et al., 2013; Shore et al., 2014 & Woo et al., 2011 & 2012) .

The meta-analysis reported pooled estimates of outcome measures at 1, 3, 6 and 12 months post-Urolift procedure. Results were shown as standardised mean gains (SMGs) rather than keeping the original units e.g. score for IPSS, ml/s for Q_{max}. Prostate symptom scores (IPSS and BPHII) are pooled and reported together, as are the sexual health scores IIEF, MSHQ-EjD and MSHQ-Bother. IPSS QoL is reported separately, as are Q_{max} and post-void residual volume (PVR). All are reported with an effect size, and a heterogeneity score.

The pooled IPSS/BPHII results presented indicate a large improvement in symptoms. The authors convert their reported SMGs into IPSS improvements as follows: -7.2 points (95% CI, -7.9 to -6.5) at 1 month, -8.3 (95% CI, -9.1 to -7.5) at 3 months, -8.7 (95% CI, -9.4 to -7.9) at 6 months and -8.0 (95% CI, -8.8 to -7.2) at 12 months. QoL measurements also improved by between 2.2 (95% CI, -2.5 to -2.0) and 2.4 points (95% CI, -2.6 to -2.2) (MG). The sexual

health scores also indicated a small improvement, SMG ranged from 0.3 (95% CI, 0.2-0.4) and 0.4 (95% CI, 0.3-0.5) .

Functional outcomes (Q_{max} and PVR) were inconsistently reported in the included studies, but Q_{max} showed a small improvement of between 3.8 ml/s (95% CI, 3.0-4.6) and 4.0 ml/s (95% CI, 3.4-4.6). The authors state that PVR results are significantly variable due to inconsitent reporting with very high heterogeneity estimates.

Summary critique of clinical evidence submitted by the sponsor

The sponsor presented a peer-reviewed systematic review (Perera et al., 2014) rather than their own literature search, data synthesis and analysis. However the systematic review included all of the studies identified as relevant by the EAC in an independent literature search.

Quality assessment of the systematic review (Perera et al., 2014) was performed by the EAC. Although some aspects of the review were reasonable there was insufficient methodological detail to fully explain their meta-analysis. Furthermore the quality of some of the included studies had a high risk of bias, 8/9 studies were uncontrolled before and after studies. Patient numbers in the analysis are not clearly explained. Perera et al., (2014) claimed that the pooled estimates were obtained from 888 to 1298 responses (depending on the score) from 452 to 680 patients. However, even if all the patients in all 10 studies listed in Table 2 are summed, this would only give 650 patients, and some of these are common to more than one study e.g. Chin et al. (2012) and Woo et al. (2012), and the two LIFT Study papers (McVary et al., 2014 & Roehrborn et al., 2013). Also the authors state that some studies were not included in the final meta-analyses, but do not clearly state which studies these are.

The results table presented gave pooled estimates of outcome measures with effect sizes, rather than using the units of individual outcome measures, which the EAC feel would be more transparent. The authors present a difference in IPSS of -7.2 and -8.7 points (a negative IPSS score is a symptom improvement). This change in IPSS is a derived number, back-calculated to IPSS scores from the effect size in the meta-analysis, which in itself is calculated from pooled IPSS and BPHII numbers. As a result, this reports a worse IPSS

improvement than in all the publications included in the meta-analysis (the EAC-calculated weighted mean IPSS score is actually around -11 points).

The potential for double-counting patients in these studies a lack of methodlogical clarity, and the somewhat short-form nature of a journal publication, means a lack of transparency in the authors' methodology for the analyses.

Summary of economic evidence submitted by the sponsor

There were no published economic studies available on the Urolift device. The sponsor's submission consisted of a very detailed de novo economic analysis and the sponsor submission was from the national NHS perspective. Data inputs for Urolift were collated from the LIFT study and expert clinical opinion. Outcome and complications costs were taken from a robust HTA (Laurenco et al. 2008).Comparators presented included TURP and HoLEP, as specified in the scope. The executable model included out-of scope-comparators such as laser resection and TUVP, which are not relevant for this assessment, but these were not included in the written submission. The time horizon was 2 years, which is appropriate, given the evidence base for Urolift.

Summary critique of economic evidence submitted by the sponsor

The sponsor's model is very thorough, and the EAC note that it actually contains too much detail e.g. out of scope comparators (laser and TUVP). The model includes before and after procedure appointments that appear to be the same for all interventions (therefore making no difference to the cost outcomesThe base case submitted actually makes Urolift slightly cost incurring (by £3 per case) versus TURP and £418 per case versus HoLEP. The sponsor's breakdown of costs for each technology showed that the equipment costs per procedure for Urolift were much greater than for the comparators. Urolift had lower clinical supplies and services costs due to the estimated shorter length of hospital stay. Sensitivity analysis was somewhat limited and a range of ±20% was insufficient for some inputs, such as LOS for Urolift, where there was considerable uncertainty.

External Assessment Centre commentary on the robustness of evidence submitted by the sponsor

The model is backed by robust data, comprising of Urolift data from the LIFT study and clinical opinion. Comparator data was taken from a thorough HTA authored by Laurenco et al. (2008). The EAC agreed with most of the inputs and assumptions used by the sponsor in the model.

Summary of any additional work carried out by the External Assessment Centre

For the clinical part of this assessment, the EAC designed and performed an independent literature search, and obtained a professional translation of the Spanish-language manuscript for Abad et al. 2013.

The EAC took a more simplified approach to the data presented in the studies for greater clarity. Firstly, we combined the three LIFT publications into a single set of results for the LIFT Study, and the two papers by Chin et al (2012) and Woo et al. (2012) to report from this 64-patient cohort. We present data as changes from baseline, with means and weighted means to account for cohort sizes, in order to retain the data in the original units. We provide context for the results by citing clinically important changes in each measure from published sources, where available, and also by surveying clinical experts. In order to provide some comparative context, we present changes from baseline in TURP and HoLEP from papers selected by a recent, methodologically robust systematic review (Li et al. 2014). It should be noted that this is not true comparative data, but gives an idea of improvements from baseline and complications post-TURP and HoLEP, presented in the same format as the Urolift data.

For the economic submission, the EAC checked the model inputs and corrected /adjusted them where necessary using a combination of published evidence and expert clinical opinion. We performed sensitivity and threshold analysis in order identify the key drivers of the model as the cost of the Urolift device, operating time and length of stay. The EAC present a scenario in which Urolift can be cost-saving compared to mTURP and BiTURP, but not HoLEP. This relies upon a low number of Urolift implants, a short procedure time of 30

minutes or less, adding urological operating theatre overhead costs, local anaesthetic, and a day-case procedure of 0.125 days (3 hours). Under these conditions, savings of £336 compared with mTURP and £209 compared with BiTURP are achievable. All of the inputs of the EAC scenario are supported by published sources or by clinical experts for the assessment, who are currently using the Urolift device in the UK.

Table 1 Glossary

Term	Definition
5-ARI	5-Alpha-Reductase Inhibitors
AUASI	American Urological Association Symptom Index (also known as IPSS score)
AUR	Acute Urinary Retention
AUS	Artificial Urinary Sphincter
BiTURP	Bipolar transurethral resection of prostate
BPH	Benign Prostatic Hyperplasia
BSC	Best Supportive Care
HOLEP	Holmium laser enucleation of the prostate
IPSS	International Prostate Symptom Score
LCI	Lower confidence interval
LOS	Length of stay
LUTS	Lower Urinary Tract Symptoms
MG	Mean Gain
mTURP	Monopolar transurethral resection of prostate
NHS	National Health System
NICE	National Institute for health and Clinical Excellence
PSA	Prostate Specific Antigen
PSS	Personal Social Services
PUL	Prostatic Urethral Lift
QALY	Quality Adjusted Life Year
RCT	Randomised Control Trial
SHIM	Sexual Health Inventory for Men (same as IIEF-5)
SMG	Standardised mean gain
TUR	Transurethral resection
TURP	Transurethral resection of the Prostate
TUVP	Transurethral Vaporisation of the Prostate
UCI	Upper confidence interval
UK	United Kingdom
UTI	Urinary tract infection

2 Background

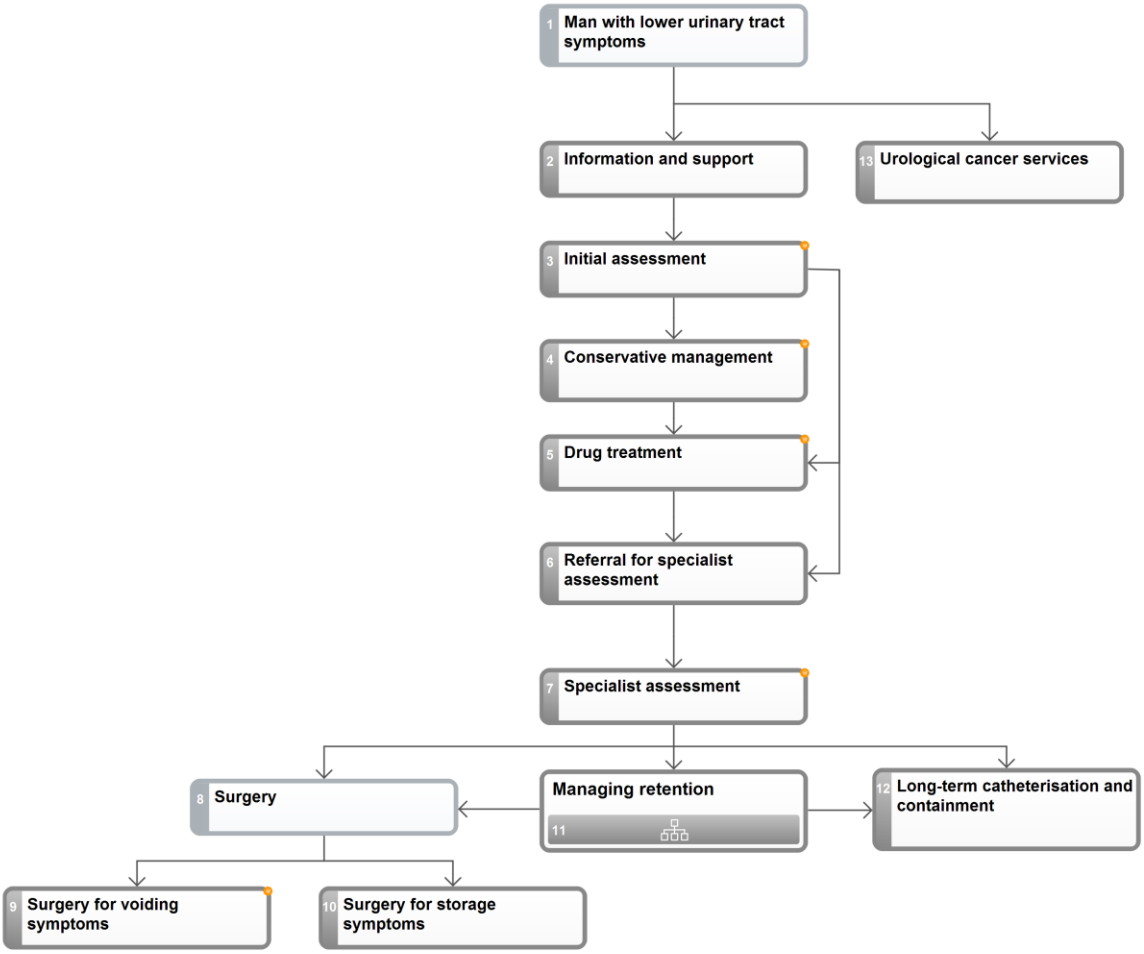
2.1 Overview and critique of sponsor's description of clinical context

The sponsor's submission outlines the clinical context well, with references from published journals to support the statements made. They describe Lower Urinary Tract Symptoms (LUTS) and the resulting decrease in quality of life that accompanies the condition. They also correctly identify that medication is the first type of therapy used to treat the condition, and that this comes with a number of unpleasant side-effects, noting that "over one quarter of patients discontinue medical therapy, often after only three months".

The sponsor refers to NICE IPG475, which has given "Normal Arrangements" for the use of prostatic urethral lift implants. It is worth noting that all the evidence in IPG475 is published data on the Urolift device, and there do not seem to be any competing devices for prostatic urethral lift.

The sponsor's submission states, "no UK clinical pathways relevant to Urolift have been published to date". However, the following overview is available on the NICE website, accompanying IPG475:

Figure 1 NICE clinical pathway for BPH



Urolift would be placed in section 9 of this pathway, as an option for "Surgery for voiding symptoms". In their submission, the sponsor specifically places Urolift in the pathway after the failure of drug management and prior to invasive surgical remedies (e.g. TURP, PVP, etc), which shows that they are aware of NICE clinical pathways and the EAC agrees that this placement of Urolift in the pathway is appropriate, as it is a minimally invasive procedure.

2.2 Overview of sponsor's description of ongoing studies

The EAC conducted an independent search of Clinicaltrials.gov and WHO International Clinical Trials Registry Platform (ICTRP), and found the same ongoing clinical trials as noted by the Sponsor in their submission. Therefore, the EAC is in agreement with the sponsor's submission. The studies found were:

1) NCT01876706. Urolift System Tolerability and ReCovery When Administering Local Anesthesia (active, not recruiting)

2) NCT01533038. BPH-6: Comparison of the Urolift System to TURP for Benign Prostatic Hyperplasia (active, not recruiting)

3) NCT01294150 . The Safety and Effectiveness of Urolift: LIFT Pivotal Study (active, not recruiting).

The EAC is particularly interested in the results, or any preliminary analyses, arising from the BPH-6 trial, as it directly compares Urolift with TURP. As such, it is the only study that fully meets the scope for this assessment. However, the Clinicaltrials.gov listing denotes an end point of December 2015 for the BPH-6 trial and trial results are not available for inclusion in this report.

2.3 Critique of sponsor's definition of the decision problem

Note: The Sponsor's submission consists of a peer-reviewed systematic review by a separate group, Perera et al. (2014), rather than a de novo literature search followed by data extraction and synthesis/meta-analysis. Where possible, we will critique the Sponsor's work, and also the systematic review by Perera et al. 2014.

2.1.1 Population

The sponsor's submission contains studies that match the requirements of the NICE scope quite well. However, in table A1, the sponsor has misunderstood the table's requirements. The aim of the table is to re-state what was asked by NICE in their scope, and then give an overview of the sponsor's presented data with a rationale for any differences presented. The sponsor used the table to outline the state of BPH more generally in the UK – describing the total patient population, the number of surgical treatments per year, and the expected outcome measurements. One point the EAC would be interested in was the rationale behind the sponsor's identification of TURP alone as the comparator to Urolift, rather than also including HoLEP, as in the NICE scope. The EAC completed the table, using the studies in the presented Perera et al. systematic review:

Table 2 EAC-completed Table A1 from sponsor submission template

	Scope issued by NICE	Variation from scope	Rationale for variation
Population	Men with lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) aged 50 or over, and with prostate volumes no greater than 100 cc (100 g).	None	
Intervention	The UroLift system	None	
Comparator(s)	Current practice varies and is changing as a result of which there are 2 comparators: Monopolar or bipolar transurethral resection of the prostate (TURP) Holmium laser enucleation of the prostate (HoLEP)	No comparative studies available – only one RCT vs sham control and uncontrolled before and after studies	No comparative studies available.
Outcomes	The outcome measures to consider include: -Length of hospital stay -The need for, or duration of, catheterisation -Number of post discharge follow-on consultations, both in primary and secondary care settings -Time to re-operation and re-operation rates -Symptoms of BPH (using the International Prostate Symptom Score [IPSS]) -Reduction in ejaculatory or sexual function -Time to return to normal	Only "Healthcare-associated infection" is not reported. UTIs, a device-related complication, are reported in the studies.	Data not available – not a standard outcome for urological studies.

	activities -Quality of life -Healthcare associated infection -Device-related adverse events		
Cost analysis	Comparator(s): Monopolar or bipolar TURP and HoLEP Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be sufficiently long to reflect any differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers and combinations of devices are needed.	Sponsor's cost model also submitted comparator costs for laser (e.g. Greenlight) transurethral vaporisation of the prostate (TUVP), and bi-TUVP.	
Subgroups to be considered	Men for whom TURP or HoLEP is unsuitable because of difficulties with blood loss or sedation.	None	
Special considerations, including issues related to equality	Men who wish to preserve sexual function and fertility.	None – sexual function scores widely reported	

2.1.2 Intervention

The sponsor's submission matches the final scope issued by NICE. The submission was restricted to Urolift, the version of the device that has received CE marking and is sold in the UK.

The procedure is undertaken transurethrally with the patient under local or general anaesthesia. A pre-loaded delivery device is passed through a rigid sheath under cystoscopic visualisation. The delivery device is used to compress one lateral lobe of the prostate in an anterolateral direction towards the prostatic capsule. A needle is then advanced through the lobe and capsule, and a monofilament implant with two end pieces is deployed. One end of the implant is anchored in the urethra and the other on the outer surface of the prostatic capsule, retracting the prostatic lobe away from the urethral lumen. Multiple implants are usually inserted during each procedure (NICE IPG475).

2.1.3 Comparator(s)

The evidence submitted by the sponsor did not include any of the comparators detailed in the final scope, the scope called for comparative evidence against TURP or HoLEP. However, all studies submitted by the sponsor were either uncontrolled before and after studies or a RCT with a sham control. However, the available evidence is limited and the EAC did not find any comparative studies with Urolift vs. TURP or HOLEP in an independent literature search. The sponsor does point out that the study populations are similar, but this is still no substitute for a true comparative (preferably blinded) study, as this can be subject to selection bias, or outcomes can be interpreted differently due to detection bias in the different populations.

2.1.4 Outcomes

Primary clinical outcomes reported in the Perera et al. (2014) systematic review were:

- Prostate symptoms (IPSS – International Prostate Symptom Score, and BPHII – BPH impact Index)
- Sexual health (IIEF – International Index of Erectile Function, MSHQ – Male Sexual Health Questionnaires for ejaculatory function for ejaculatory function and Bother)
- Functional parameters (Qmax – maximum urinary flow rate, and PVR – post void residual volume)
- Procedural data (local anaesthetic, operative time and number of Urolift implants used
- Time to re-operation, reported as “progression to TURP at 12 months”
- Postoperative catheterisation

- Early postoperative complications, dysuria, haematuria, pelvic pain, urinary tract infection, incontinence)
- Device-related adverse events

The final scope listed additional outcomes, which were not reported in any of the identified studies. These were:

- Length of hospital stay
- Number of post-discharge follow-on consultations
- Time to return to normal activities

2.1.5 Cost analysis

The cost analysis presented in the sponsor's submission was a very detailed de novo economic analysis that matched the analysis specified in the scope. Costs were presented from national NHS perspective. Comparators presented included TURP and HoLEP, as specified in the scope. The time horizon is 2 years, which is appropriate, given the evidence base for Urolift, and outcome and complications are costed from a thorough HTA (Laurenco et al. 2008).

2.1.6 Subgroups

The scope specifies subgroups as men for whom, TURP or HoLEP is unsuitable because of difficulties with blood loss or sedation. Blood loss is not directly reported in the manufacturer's submission, but some of the identified studies report transfusion rates as a complication of the Urolift procedure. The EAC note that this technology may be of a benefit to groups for whom blood transfusions are not an option e.g. Jehovah's Witnesses.

Sedation data (local versus general anaesthetic) is also addressed by a number of the publications.

2.1.7 Special considerations, including issues related to equality

Special considerations in the scope were for men who wished to preserve sexual function and fertility. Several of the papers in the systematic review had contained outcomes pertaining to sexual function, which addresses this concern.

No equality issues were identified in the scope. Neither the sponsor nor the EAC have identified any further equalities issues.

3 Clinical evidence

Note: The Sponsor did not present a de novo literature search and review for their clinical submission of evidence. A systematic review by Perera et al. (2014) was presented instead. The systematic review (Perera et al. (2014) included 10 studies: two reports from an RCT and eight uncontrolled before and after studies.

3.1 Critique of the sponsor's search strategy

As noted above the sponsor did not undertake their own literature search. Instead, the sponsor described the literature search methods that were used in a recent, peer-reviewed systematic review (Perera et al. 2014). The search strategy is provided in the supplementary data that accompanies the systematic review publication. The EAC critically appraised the systematic review (Perera et al. 2013) using a checklist designed by the Support Unit for Research Evidence, Cardiff University.

The scope of the systematic review (Perera et al., 2014) lacked detail with regard to the population and comparators. The search strategy of the review was appropriate and the sources searched provided reasonable coverage for the review itself. However the review did not include a search for clinical trials, adverse events or seek to obtain unpublished data all of which are required for a submission of evidence. The sponsor attempted to seek unpublished data though this did not include contacting the authors of the included studies. The EAC designed a search strategy and performed an independent search of the literature, details in 3.9.

3.2 Critique of the sponsor's study selection

Inclusion and exclusion criteria were briefly described, and copied directly from the methods section of Perera et al. (2104). Studies reporting functional sexual outcomes following the urethral lift procedure for LUTS secondary to BPE were included. No language or sample-size restrictions were used. Conference proceedings were not included.

For publications where duplicate study populations or repeated data were identified, the publications reporting the larger sample size was used. However, due to the lack of

transparency in the methods presented by the Sponsor (specifically in the meta-analysis), the EAC took a more simplified approach to the analysis of data presented in the studies. Certain publications (Chin et al., 2012 and Woo et al., 2012, and those reporting the LIFT Study) were collated together to avoid double-reporting of results from the same patient cohorts (see section 3.9 – Additional work carried out by the EAC).

3.3 Included and excluded studies

Of 61 suitable studies, 23 conference proceedings and 28 editorials were excluded by Perera et al. (2014). One published study (Abad et al. 2013) was also excluded, as it did not report standard deviations. Nine studies were finally included:

Table 3 Included and excluded studies

Study	Country	Study Description	S quality assessment system ample size
Abad et al. 2013 (**excluded by Sponsor**)	Spain	Uncontrolled before and after study	20
Cantwell et al., 2013	,USA, Canada and Australia. 19 centre study	Before and after study to assess Urolift in patients who had previously been randomised to the sham arm of the LIFT study. After the primary endpoint comparison at 3 months, sham controls were unblinded and offered enrolment into this study.	53 (patients elected to have PUL after sham in the LIFT study)
Chin et al. , 2012 (same cohort as Woo et al. 2012 – see below)	Australia 6 centre study	Multicentre uncontrolled before and after study.	64
Delongchamps et al., 2012	France	Single centre prospective uncontrolled before and after study.	4
Roehrborn et al., 2013 (LIFT Study)	19 centre study: USA 14 Canada 2 Australia 3	RCT, 2:1 randomisation between Urolift and sham control. Sham control: patient blinded and given rigid cystoscopy, no implants used.	Urolift group: 140 Control group: 66
McVary et al., 2014 (LIFT Study)	19 centre study: USA 14 Canada 2 Australia 3	RCT, 2:1 randomisation between Urolift and sham control. Sham control: patient blinded and given rigid cystoscopy, no implants used.	Urolift group: 140 Control group: 66
McNicholas et al., 2013	7 centres in 5 countries. Not clearly stated, authors are from UK, Australia, USA, Spain, Germany,	Retrospective analysis of prospectively accrued data from consecutive multicentre uncontrolled before and after study.	102

	The Netherlands and Italy.		
Shore et al., 2014	Not reported	Uncontrolled before and after study.	51
Woo et al., 2011	Australia	Prospective, non-randomised uncontrolled before and after study, assessing safety and feasibility.	19
Woo et al., 2012 (same cohort as Chin et al. 2012 – see above)	Australia 6 centre study	Multicentre uncontrolled before and after study.	64

The EAC's independent literature search did not find any additional studies over those found by the sponsor. Alongside the systematic review by Perera et al. (2014), the sponsor also provided one additional publication: a 2-year update on the LIFT Study by Roehrborn et al. 2014. The sponsor states "the results do not materially change the meta-analysis and thus Perera et al. (2014) stands as relevant and current".

Delongchamps et al. (2012), a study published in French with only 4 patients, was excluded as it was not considered to be a pivotal study for this assessment.

Summary of the key points in each study:

Abad et al. (2013) (Not included in Sponsor's meta-analysis):

Patient population	Sample size		Country	Mean age±SD	Mean baseline IPSS, or BHPII ±SD	Mean baseline IIEF or MSHQ ±SD	Mean baseline Qmax ±SD	Mean baseline prostate volume ±SD	Mean baseline PVR ±SD	Study design
Inclusion criteria: Age ≥50, IPSS >20, Qmax <15ml/s, PSA<10 ng/ml **Exclusion criteria:** Obstructing medial lobe (observed with cystoscopy), urinary tract infection, previous surgical treatment for prostate pathology.	**Urolift group:** 20 **Withdrawals:** None **Note:** No SDs reported for baselines or results.		Spain	Mean 74.3 (range 43-90) years	IPSS 26.7, (range 20-35)	Not reported	All patients: Mean 6.9 (range 0-13 ml/s Excluding 4 patients catheterised at baseline due to chronic retention: Mean 8.6ml/s (range 3-13)	42.6 (range 19-109) cc (TRUS)	Not reported	Retrospective uncontrolled before and after study. Primary endpoints: evaluate the effectiveness of Urolift and the number and intensity of side effects post-procedure **Follow-up:** IPSS, BPHII and Qmax at 4 weeks, 3, 6 and 12 months.

Cantwell et al. (2013):

Patient population	Sample size	Country	Mean age±SD	Mean baseline IPSS, or BHPII ±SD	Mean baseline IIEF or MSHQ ±SD	Mean baseline Qmax ±SD	Mean baseline prostate volume ±SD	Mean baseline PVR ±SD	Study design
Inclusion criteria: ≥50 years old, provided informed consent, no prior surgical BPH treatment, washed out or naive to α-blockers or 5 α-reductase inhibitors. IPSS ≥13, Qmax ≤12ml/s with a voided volume of 125ml. Prostate volume of 30-80ml, without an obstructing median lobe. **Exclusion criteria:** Retention, post-void residual volume (PVR) >250ml, active infection, PSA >10ng/ml unless negative biopsy, cystolithiasis within 3 months, bacterial prostatitis within 1 year.	53 patients elected to have PUL after sham in the LIFT study. **Withdrawals:** None	19 centre study, USA, Canada and Australia.	64±8.0, range 50-79) years	IPSS 23.3±5.5, (range 13-34) IPSS QoL 4.5±1.2 (range 2-6) BPHII (n=52) 6.3±3.0 (range 1-12)	IIEF (n=53) 12.8±8.3, (range 1-25) MSHQ-EjD (n=42) 9.5±10.0 (range 3-14)	.8±4.2 (range 2.0-30.0) ml/s	40.3±9.9 (range 30-68) mls	67.8±66.44 (range 0-262) mls	Before and after study to assess Urolift in patients who had previously been randomised to the sham arm of the LIFT study. Primary endpoints were symptom scores, QoL and sexual health questionnaire scores. **Follow-up:** IPSS, IPSS QoL BPHII, IIEF-5 and MSHQ were 2 weeks, 1, 3, 6 and 12 months. Qmax and PVR at 3 and 12 months. Safety was assessed at each follow-up visit

Chin et al. (2013)

Patient population	Sample size	Country	Mean age±SD	Mean baseline IPSS, or BHPII ±SD	Mean baseline IIEF or MSHQ ±SD	Mean baseline Qmax ±SD	Mean baseline prostate volume ±SD	Mean baseline PVR ±SD	Study design
Inclusion criteria: ≥55 years of age,. Symptomatic BPH, IPSS>13, PVR<250ml, peak Qmax of 5-12ml/s. Wash-out of α-blockers for 1 week and 5 α-reductase inhibitors within 6 months of treatment. **Exclusion criteria:** PSA >10ng/ml, history of urinary retention, previous prostate surgery, compromised renal function, current infection, obstructive median lobes.	**Urolift group:** 64 **Withdrawals:** Not reported	Australia (6 different centres)	66.9 ±7.3 years (range 53-83)	IPSS: Not reported for total cohort, but varies throughout follow-up Duration of LUTS = 4.7±4.3 years (range 0.5-23)	Not reported for total cohort, but varies throughout follow-up	Not reported for total cohort, but varies throughout follow-up	51 ±23 mls (range 21-149) (TRUS)	Not reported for total cohort, but varies throughout follow-up	Multicentre uncontrolled before and after study. Primary endpoints were longer-term effectiveness of PUL in relieving LUTS **Follow-up:** 2 weeks, and 3,6,12 and 24 months IPSS results were analysed on a) the entire dataset and b) patients 26-64 only. Patients 26-64 had the most recent version of Urolift device (3 generations of device used over the total cohort) and refined method used, where implant placement formed continuous channel from bladder neck to verumontanum.

Roerhborn et al. 2013 (the LIFT Study):

Patient population	Sample size	Country	Mean age±SD	Mean baseline IPSS, or BHPII ±SD	Mean baseline IIEF or MSHQ ±SD	Mean baseline Qmax ±SD	Mean baseline prostate volume ±SD	Mean baseline PVR ±SD	Study design
Inclusion criteria ≥50 years of age, provided consent, , no prior BPH surgical treatment, washout of 2 weeks for α-blockers, 3 months for 5-α-reductase inhibitors, 3 days for anticoagulants, IPSS>13, Qmax ≤12ml/s, 125ml voided volume, 30-80cc prostate volume (via TRUS). **Exclusion criteria:** Median lobe obstruction, retention, PVR >250ml, active infection, PSA >10ng/ml (unless negative biopsy), cystolithiasis within 3 months and bacterial prostatitis within 1 year.	**Urolift group:** 140 **Ctrl group:** 66 **Withdrawals:** 7 censored due to use of BPH medication 1 subject discontinued participation 2 exclusions due to significant protocol violations	19 centres: USA 14 Canada 2 Australia 3	**Urolift group:** 67±8.6 years **Ctrl group:** 65±8.0 years	**Urolift group:** IPSS 22.2±5.4 **Ctrl group:** Mean 24.4±5.8 **Urolift group:** IPSS QoL 4.6±1.1 **Ctrl group:** IPSS QoL 4.7±1.1 BPHII baselines not reported	**Urolift group:** IIEF 13.0±8.4 MSHQ-EjD 8.7±3.2 **Ctrl group:** IIEF 13.5±8.5 MSHQ-EjD 8.8±3.2	**Urolift group:** 8.9±2.2 ml/s **Ctrl group:** 8.8±2.2 ml/s	**Urolift group:** 44.5±12.4 mls **Ctrl group:** 40.9± 10.8 mls	**Urolift group:** 85.5±69.2 mls **Ctrl group:** 87.7± 72.4 mls	RCT, 2:1 randomisation between Urolift and sham control. Sham control: patient blinded and given rigid cystoscopy, no implants used. Primary endpoint: reduction in IPSS at 3 months after PUL procedure was at least 25% better than sham. **Follow-up:** IPSS, QoL, BPHII, IIEF and MSHQ-EjD assessed at 2 weeks, 1,3, 6,12 and 24 months.

McNicholas et al. 2013

Patient population	Sample size	Country	Mean age±SD	Mean baseline IPSS, or BHPII ±SD	Mean baseline IIEF or MSHQ ±SD	Mean baseline Qmax ±SD	Mean baseline prostate volume ±SD	Mean baseline PVR ±SD	Study design
Inclusion criteria: Prostate volume <60mls, IPSS>12, Qmax<15ml/s, PVR<350 NOTE: these are "typical inclusions" No exclusion criteria reported	102	7 centres in 5 countries. Not clearly stated, authors are from UK, Australia, USA, Spain, Germany, The Netherlands and Italy.	Mean 68±10 years	IPSS 23.2±6.1 IPSS QoL 4.7±1.0	Not reported for total cohort, but varies throughout follow-up	8.7±4.0 ml/s	48±21mls	Not reported for total cohort, but varies throughout follow-up	Retrospective analysis of prospectively accrued data from consecutive uncontrolled before and after study. Primary endpoints were to evaluate safety and efficacy with the most current Urolift device and surgical technique in day-to-day practice. **Follow-up:** 2 and 6 weeks, 3,6 and 12 months

McVary et al. 2014 (the LIFT Study):

Patient population	Sample size	Country	Mean age ±SD	Mean baseline IPSS, or BHPII ±SD	Mean baseline IIEF or MSHQ ±SD	Mean baseline Qmax ±SD	Mean baseline prostate volume ±SD	Mean baseline PVR ±SD	Study design
Inclusion criteria >50 years of age, provided consent, , no prior BPH surgical treatment, washout of 2 weeks for α-blockers, 3 months for 5-α-reductase inhibitors, 3 days for anticoagulants, IPSS ≥13, Qmax ≤12ml/s, 125ml voided volume, 30-80cc prostate volume (via TRUS). **Exclusion criteria:** Median lobe obstruction, retention, PVR >250ml, active infection, PSA >10ng/ml (unless negative biopsy), cystolithiasis within 3 months and bacterial prostatitis within 1 year.	**Urolift group:** 140 **Ctrl group:** 66 **Withdrawals:** 7 censored due to use of BPH medication 1 subject discontinued participation 2 exclusions due to significant protocol violations	19 centres: USA 14 Canada 2 Australia 3	**Urolift group:** 67 years **Ctrl group:** 65 years **Note:** SDs not reported by McVary but cohort is the same as Roerhborn et al. 2013 above.	**Urolift group:** IPSS 22 **Ctrl group:** IPSS 24 **Urolift group:** IPSS QoL 4.6 **Ctrl group:** IPSS QoL 4.7	**Urolift group:** IIEF 13.0 **Ctrl group:** IIEF 13.5	**Urolift group:** 8.9 ml/s **Ctrl group:** 8.8 ml/s	Not reported	Not reported	RCT, 2:1 randomisation between Urolift and sham control. Shame control: patient blinded and given rigid cystoscopy, no implants used. **Primary endpoint:** Change in IPSS and sexual health measures (IIEF and MSHQ) up to 12 months post-PUL **Follow-up:** QoL, BPHII, IIEF and MSHQ-EjD assessed at 2 weeks, 1,3,6,12 and 24 months.

Shore et al. 2014:

Patient population	Sample size	Country	Mean age±SD	Mean baseline IPSS, or BHPII ±SD	Mean baseline IIEF or MSHQ ±SD	Mean baseline Qmax ±SD	Mean baseline prostate volume ±SD	Mean baseline PVR ±SD	Study design
Inclusion criteria: ≥50 years of age, provided informed written consent, had no prior surgical BPH treatment, wased out or naive to α-blockers and 5- α-reductase inhibitors. IPSS ≥13. Qmax <12ml/s, prostate volume 30-80cc without obstructing median lobe. **Exclusion criteria:** Current urinary retention, PVR >250ml, active infection, gross haematuria, cystolithiasis, within 3 months, bacterial prostatitis within 1 year.	51	NR	66±7.6 years (range 51-85)	IPSS 21.45±5.43 (range 13-32) BPHII 6.65±3.08	IIEF 16.51±7.33 ml/s (range 2-25) MSHQ-EjD 9.95±2.59 (range 5-15)	8.22±2.18 (range 2-12.0)	41.3±11.6 cc (range 30.0-77.3)	77.05±74.92 mls (range 0-247)	Non-blinded uncontrolled before and after study. **Primary endpoint:** ascertain whether 80% of patients achieve a score of ≥80 on the Quality of Recovery Visual Analogue Scale (QoR VAS) by 1 month follow-up. **Follow-up:** 2 weeks, and 1 month

Woo et al. 2011:

Patient population	Sample size	Country	Age±SD	Mean baseline IPSS, or BHPII ±SD	Mean baseline IIEF or MSHQ ±SD	Mean baseline Qmax ±SD	Mean baseline prostate volume ±SD	Mean baseline PVR ±SD	Study design
Inclusion criteria: IPSS ≥13, Qmax 5-12ml/s, prostate volume 20-100ml, PVR <250ml, PSA <10ng/ml. **Exclusion criteria:** Median lobe obstruction, current infection, history of urinary retention, α-adrenergic receptor blocking medication within 1 week, or 5-α-reductase inhibitor medication within 6 months of treatment, history of significant medical co-morbidity, prior BPH surgery, or if had a known or suspected urological condition that may affect voiding function.	19	Australia	Mean 66±6 years (range 55-77)	Not reported for total cohort, but varies throughout follow-up	Not reported	Not reported for total cohort, but varies throughout follow-up	Mean 49±20 mls (range 21-97)	Not reported for total cohort, but varies throughout follow-up	Prospective, non-randomised safety and feasibility study **Primary aim:** Safety: Evaluate number and severity of SAEs up to 12 months follow-up Feasibility: deliver sutures to increase urethral lumen **Follow-up:** IPSS and QoL at 2 weeks, 3, 6 and 12 months

Woo et al. 2012:

Patient population	Sample size	Country	Age±SD	Mean baseline IPSS, or BHPII ±SD	Mean baseline IIEF or MSHQ ±SD	Mean baseline Qmax ±SD	Mean baseline prostate volume ±SD	Mean baseline PVR ±SD	Study design
Inclusion criteria: ≥55 years of age,. Symptomatic BPH, IPSS>13, PVR<250ml, peak Qmax of 5-12ml/s. Wash-out of α-blockers for 1 week and 5 α-reductase inhibitors within 6 months of treatment. **Exclusion criteria:** PSA >10ng/ml, history of urinary retention, previous prostate surgery, compromised renal function, current infection, obstructive median lobes.	**Urolift group:** 64 **Withdrawals:** Not reported	Australia (6 different centres)	66.9 ±7.3 years (range 53-83)	**IPSS:** 22.9 ±5.4 (range 14-35, n=64) **Duration of LUTS** = 4.7±4.3 years	**IIEF:** 11.7(±8.6) (range 1-25, n=58) **MSHQ-EjD:** 9.0±3.7 (range 1-15, n=46) **MSHQ-Bother:** 1.7 ±1.5 (range 0-5 , n=46)	Not reported	51 ±23 mls (range 21-149) (TRUS)	Not reported	Multicentre uncontrolled before and after study. Primary endpoint: effect of PUL on erectile and ejaculatory function **Follow-up:** 2 weeks, and 3,6, and 12 months

3.4 Overview of methodologies of all included studies

Table 4 Overview of methodologies of all studies

Study	Methods
Abad et al. 2013 (not included in Sponsor's submission)	**Primary endpoints:** Evaluate the effectiveness of Urolift and the number and intensity of side effects post-procedure **Follow-up:** IPSS, BPHII and Qmax at 4 weeks, 3, 6 and 12 months. **Statistical methods:** Changes from baseline measurements compared and Wilcoxon nonparametric test used. Significance calculated as $p<0.05$.
Cantwell et al. 2013	**Primary endpoints:** Symptom scores, QoL and sexual health questionnaire scores. **Follow-up:** IPSS, IPSS QoL and BPHII were assessed at 2 weeks, 1 and 3 months after both the sham and PUL and additionally at 6 and 12 months post-PUL. IIEF-5, MSHQ-EjD and MSHQ-Bother were also assessed at the same time-points in sexually active patients. Qmax and PVR assessed at 3 and 12 months. Safety was assessed at each follow-up visit through adverse event reporting. **Statistical methods:** Descriptive statistics used for IPSS, IPSS QoL, BPHII, Qmax, PVR, IIEF-5, MSHQ-EjD. Students t-test used to compare changes from baseline to 3 months between sham and PUL.
Chin et al. 2012	**Primary endpoints:** longer-term effectiveness of PUL in relieving LUTS **Follow-up:** 2 weeks, and 3,6,12 and 24 months **Statistical methods:** To evaluate change from baseline, a general estimating equation model was fit to each outcome parameter (IPSS, QoL, BPHII, Qmax, PVR, IIEF (SHIM) and MSHQ-EjD). To address potential effects of the device and procedural changes made during the study, IPSS results were analysed on a) the entire dataset and b) patients 26-64 only.
Roehrborn et al. 2013 (The LIFT Study)	**Primary endpoint:** Reduction in AUASI (IPSS, on an intention-to-treat basis) at 3 months after PUL procedure was at least 25% better than sham. **Follow-up:** QoL, BPHII, IIEF and MSHQ-EjD assessed at 2 weeks, 1,3,6,12 months. **Statistical methods:** The study was powered for the primary endpoint assuming a Student's *t* test comparison of mean values on an ITT basis, 0.05 2-sided type-1 error and 80% power. For per-protocol analysis to evaluate change from baseline, a general estimating equation model was fit to each outcome parameter.
McVary et al. 2013 (The LIFT Study)	**Primary endpoint:** Change in IPSS and sexual health measures (IIEF and MSHQ) up to 12 months post-PUL **Follow-up:** QoL, BPHII, IIEF and MSHQ-EjD assessed at 2 weeks, 1,3,6, and 12 months. **Statistical methods:** The study was powered for the primary endpoint assuming a Student's *t* test comparison of mean values on an ITT basis, 0.05 2-sided type-1 error and 80% power. For per-protocol analysis to evaluate change from baseline, a general estimating equation model was fit to each outcome parameter.
McNicholas et al. 2013	**Primary endpoints**: Evaluate safety and efficacy with the most current Urolift device and surgical technique in day-to-day practice. **Follow-up:** 2 and 6 weeks, 3,6 and 12 months **Statistical methods:** To evaluate change from baseline, a general estimating equation model was fit to each outcome parameter (IPSS, QoL, BPHII, Qmax, PVR, IIEF (SHIM) and MSHQ-EjD).
Shore et al. 2014	**Primary endpoint:** Ascertain whether 80% of patients achieve a score of ≥80 on the Quality of Recovery Visual Analogue Scale (QoR VAS) by 1-month follow-up. **Follow-up:** 2 weeks, and 1 month **Statistical methods:** Primary endpoint tested by calculating the one-sided 95% confidence

	limit using the Clopper-Pearson method. Descriptive statistics used for IPSS, IPSS QoL, BPHII, Qmax, PVR, IIEF-5, MSHQ-EjD. A general estimating equation model was fit to each outcome parameter.
Woo et al. 2011	**Primary aims:** Safety: Evaluate number and severity of SAEs up to 12 months follow-up Feasibility: deliver sutures to increase urethral lumen **Follow-up:** IPSS and QoL at 2 weeks, 3, 6 and 12 months **Statistical methods:** Not reported.
Woo et al. 2012	**Primary endpoints:** Effect of PUL on erectile and ejaculatory function **Follow-up:** 2 weeks, and 3,6,and 12 months **Statistical methods:** To evaluate change from baseline, a general estimating equation model was fit to each outcome parameter (IPSS, QoL, BPHII, Qmax, PVR, IIEF (SHIM) and MSHQ-EjD). To address potential effects of the device and procedural changes made during the study, IPSS results were analysed on a) the entire dataset and b) patients 26-64 only.

3.5 Overview and critique of the sponsor's critical appraisal

The sponsor's submission contained a number of tables with critical appraisals for the studies within the Perera et. al. systematic review. The table template used was designated for randomised controlled trial (RCT) appraisal, and appropriately used for the two LIFT Study papers (Roerhborn et al. 2013 and McVary et al. 2014). All other studies are uncontrolled before and after studies and were appraised appropriately with a tool for observational studies.

Quality assessment in the systematic review by Perera et al. (2014) is described very briefly. Studies were quality assessed by two researchers, working independently, using a method based on The Cochrane Handbook for Systematic Reviews of Interventions 5.02.

3.6 Results

Table 5 Sponsor's submission meta-analysis results, as presented in Perera et al. 2014

	1 month	3 month	12 month	24 month
Prostate symptom scores (IPSS, BPHII) No of data sources, response sample size (*n*)	9 (1298)	6 (1050)	6(1022)	6 (888)
Effect size (95% CI)	-1.30 (-1.4 to -1.2)	-1.50 (-1.7 to -1.4)	-1.6 (-1.7 to -1.3)	-1.5 (-1.6 to -1.3)
Heterogeneity (τ^2)	0.1	0.1	0.00	0.00
Male sexual health scores (IIEF, MSHQ-EjD, MSHQ-Bother) No of data sources, response sample size (*n*)	13 (1042)	9 (889)	9 (908)	9 (786)
Effect size (95% CI)	0.4 (0.3 to 0.5)	0.4 (0.3 to 0.5)	0.4 (0.3 to 0.5)	0.3 (0.2 to 0.4)
Heterogeneity (τ^2)	0.00	0.00	0.00	0.00
Health related QoL No of data sources, response sample size (*n*)	4 (628)	3 (508)	3 (496)	4 (452)
Effect size (95% CI)	-2.2 (-2.5 to -2.0)	-2.4 (-2.6 to -2.2)	-2.4 (-2.6 to -2.2)	-2.2 (-2.4 to -2.1)
Heterogeneity (τ^2)	0.2	0.1	0.1	0.00
Maximum flow rate (Qmax) No of data sources, response sample size (*n*)	3 (242)	3 (488)	1 (106)	3 (362)
Effect size (95% CI)	3.8 (3.0 to 4.6)	4.0 (3.4 to 4.6)	4.4 (3.2 to 5.6)	3.8 (3.1 to 4.4)
Heterogeneity (τ^2)	0.4	0.03	NA	0.2
Postvoid residual (PVR) No of data sources, response sample size (*n*)	2 (128)	2 (396)	1 (122) Note: this is data from a single study	2 (350)
Effect size (95% CI)	15.5 (12.6 to 18.6)	-6.2 (-10.1 to -2.8)	-11 (-13 to -9)	-4.0 (-10.5 to 2.6)
Heterogeneity (τ^2)	1732	24	NA	219

The presentation of the meta-analysis makes it difficult to elucidate which studies are being used by the sponsor, as it is not explicitly stated. The number of studies using different outcome measures varies but exact studies are not identified by name.

Raw data are not presented at all, and therefore this is difficult to discuss, as the results are presented in meta-analysis form only, with a separate table for collated complications (see Section 3.7 below).

Each study does contain the relevant patient population (elucidated by the EAC after gathering the included papers), and uses Urolift as the intervention, which is within scope.

There were no comparators (the scope required comparative studies with TURP or HoLEP, as discussed previously) because identified studies were either case series or a single RCT against a sham control. No comparative studies for Urolift against TURP or HoLEP exist at the time of writing.

The lack of detail in the results presentation in the sponsor's submission means that it is more appropriate to critique the meta-analysis by Perera et al. – see Section 3.8.

3.7 Description of the adverse events reported by the sponsor

The operative details and complications are reported in one unified table that the sponsor presented from Perera et al. (2014). Complications are not combined, but reported for each publication separately.

Operative details are:

- Local anaesthetic (incidence of use), operative time (mins), implants (meaning number of Urolift implant sutures used in the procedure), postoperative catheter (patient numbers needing catheterisation, or catheterised as per hospital protocol).

Complications reported are:

- Early postoperative complications:
    - Dysuria, haematuria, pelvic pain, UTI (urinary tract infection), Incontinence
- Progression to TURP at 12 months

The EAC feels that the adverse events reported are quite mild, with the most common complications being short-term dysuria and haematuria.

One item of greater concern is the variability in progression to TURP at 12 months – this is reported as being as low as 1.4% (LIFT Study, Roerhborn et al. 2013) but as high as 19% (Chin et al. 2012).

The authors also mention implant encrustation and quantify it in the text of the review. This is reported in one of the studies (publications by Chin et al. 2012 and Woo et al 2012), and

occurs when implants are placed too close to the bladder, exposed to static urine. Two out of fourteen encrusted implants required removal with endoscopic forceps. This is important as a Urolift-specific complication that will not arise with TURP or HoLEP. In order to get more detail on this issue, the EAC consulted clinical experts on the severity of implant encrustation. The opinions varied due to there being very little long-term data available on Urolift. Three experts stated that encrustation is a significant issue, with one detailing that they will gradually become stones over time, potentially causing an infection. Two experts did not see encrustation as a significant issue, and one further expert stated that he did not know due to lack of long-term data. The majority of experts stated that the removal of encrusted implants was a simple procedure, but one expert was concerned that a TURP or HoLEP to remove encrusted implants was more complex than a standard procedure.

The EAC were also concerned that the Urolift implants themselves may cause a problem if a patient progresses to TURP. This may be through conduction of heat or electricity from the electrosurgery loop. The EAC asked Specialist advisers about this issue, and were reassured that it is not a concern, particularly from Specialists who had performed a post-Urolift TURP in practice. One published source (Woo et al. 2011) mentions that three patients in their case series required TURP and the Urolift implants were cut without difficulty and no alteration of the TURP procedure was required. This was also the case in Chin et al. 2012, where patients were re-treated with TURP, photoselective vaporisation of the prostate or repeat Urolift procedure. Each retreatment method was performed routinely, unaffected by the presence of the Urolift implants.

Our EAC data analysis shows that not all complications are reported in the systematic review, so we will attempt to rectify this in Section 3.9.

3.8 Description and critique of evidence synthesis and meta-analysis carried out by the sponsor

The meta-analysis results presented by the sponsor are shown in Section 3.7 and are the only (non-complication) outcome measure results in Perera et al. (2014).

The systematic review gives insufficient methodological detail to fully explain their meta-analysis. The results table presented gives pooled estimates of outcome measures with

effect sizes, rather than using the units of individual outcome measures, which the EAC feel would be more transparent. Below are categorised notes on the meta-analysis:

Patient numbers

The authors claimed that the pooled estimates were obtained from 888 to 1298 responses (depending on the score) from 452 to 680 patients. However, even if all the patients in all 10 studies listed in Table 2 are summed, this would only give 650 patients, and some of these are common to more than one study e.g. Chin et al 2012 and Woo et al. 2012, and the two LIFT Study papers (and this despite the fact that the authors stated that some studies were not included in the final meta-analyses). The EAC has attempted to contact the authors regarding this issue but received no response.

Making an assumption of which five studies were included in the final meta-analyses gives a total number of 53 (Cantwell et al., 2014) + 140 [Lift Study (McVary et al., 2014 & Roehrborn et al., 2013)] + 51 (Shore et al., 2014) + 102 (McNicholas et al., 2013) + 64 (Chin et al. 2012) = 410 patients, much less than the numbers quoted by the authors.

Further, in Table 4, the number of studies included in the analysis in many of the cells exceeds either 5 or 6, with up to 13 studies being included for one analysis (with 1042 responses). It is not clear which studies have been included in each of the analyses.

Note that in the abstract, it is stated that 6 independent patient cohorts were included for analysis, although the conclusions state 5.

Presentation of meta-analyses

Presumably, the primary outcome of interest is the change in IPSS and whether there is a significant improvement; or, alternatively, whether the improvement is similar to that found when using other established methods, but with fewer side effects.

However, the Perera et al. (2014) present the outcome as a compound 'prostate symptom score' (IPSS and BPHII combined) in Figure 2 and Table 4, so it is difficult (if not impossible) to determine how much the IPSS itself has changed following the procedure.

The authors present in the abstract that there was a difference in IPSS of -7.2 to -8.7 points, but with no indication if this is a range, a confidence interval or at which time-point(s). In the discussion, this is stated as an improvement of -8.0 points (95% CI, -8.8 to -7.2) at 12-mo follow-up. In fact, the change in IPSS is a derived number, calculated as follows (according to *Data extraction and analysis*):

The standardised mean gain (SMG) was calculated from the pooled standard deviation of the multiple scales comprising the prostate symptom score. The SMG and its 95% CI were then multiplied by 5.5, which 'represents a typical standard deviation for the IPSS scores'. Moreover, the authors state that 'This interpretation should be considered indicative only'. This caution is not repeated in the abstract or the discussion. This method of calculation seems to be unwarranted when the actual IPSS scores, their means and overall changes, could be presented.

The usual method used to present results from a meta-analysis (using forest and funnel plots) was not used by the authors. For example, if the outcome of interest is the change in IPSS 3 months after the procedure, then (as an example) the results from McVary and Cantwell (and others) could be combined. Separately, the results are as follows:

Table 6 Calculation of 95% CI of mean change after 3 months in IPSS from two studies on PUL

Paper	Mean change (SD)	n	95% CI
McVary	-11.1 (7.67)	140	-9.8 to -12.4
Cantwell	-11.1 (7.2)	52	-9.1 to -13.1

Note that Perera et al. (2014) state that a difference in IPSS of 7 points represents a large difference. Not only is the mean change in IPSS greater than 7 in both these studies, but the whole 95% confidence interval is also greater than 7. Therefore, the results from just these two studies indicate a statistically significant and clinically important effect of the procedure on the IPSS score (in fact, not only are the mean changes statistically significantly different to zero, ruling out the null hypothesis, but they are also significantly different to 7).

Note also that the mean change is identical in both studies, although the patients are drawn from the same study population. One reason for carrying out a meta-analysis is to see if the effect of the treatment is similar in different populations, but the results from the individual studies would have to be displayed in order to provide this information. Another reason for carrying out a meta-analysis is to combine results from several underpowered studies to provide a robust estimation of the effect of a particular treatment. However, in this case, it appears that the individual studies have already demonstrated a significant effect (statistically and clinically) of the treatment.

Other (minor) comments

Most of the studies in the meta-analysis were uncontrolled studies, with a single sham-control RCT. It may not be appropriate to present effect-size data from non-comparative studies in this way, as this type of meta-analysis is typically reserved for two-armed randomised trials.

Heterogeneity is usually expressed using I^2, which varies in value between 0 and 100%. However, in this study, heterogeneity was expressed in terms of τ^2, which is usually used to express an estimate of the between-study variance in a random-effects meta-analysis.

The authors claimed that the mean operative time was comparable over the six patient series, but the values stated were 19.1 to 66 minutes, which appears to indicate a large difference between studies.

3.9 Additional work carried out by the External Assessment Centre in relation to clinical evidence

EAC literature search

The EAC designed a search strategy in Medline (Ovid), (Appendix 1) and conducted a search of Medline and Medline In-Process. The strategy was adapted for and run in the following databases:EMBASE; The Cochrane Library; Pubmed (“epub ahead of print”); National Technical Information Service (NTIS) database; NHS Evidence and Web of Science Core

Collection. Citation tracking in Google Scholar of the studies included in the Perera et al. (2014) review was also performed.

The EAC conducted a search of the FDA MAUDE database and of the MHRA Field Safety Notices and Medical Device Alerts for adverse events and safety alerts and warnings related to Urolift, none were identified. No additional adverse events were detailed in the publications found by the EAC.

The EAC search identified all studies included in the Perera et al. (2014) review as well as editorials, conference proceedings and reviews that referenced the sponsor-submitted studies (and therefore carried no additional value, and were not included) but no other additional studies that met the inclusion criteria were identified. The sponsor also provided a more recent two-year follow-up of the LIFT Study by Roehrborn et al. 2014. Expert clinical advisers requested long-term data in this Assessment, so these results were incorporated into the EAC's analysis.

Specifically no comparative studies of Urolift vs. TURP/HoLEP were identified by the EAC, which would have more closely fit the NICE scope for this assessment. No additional adverse events were detailed in the publications found by the EAC.

We obtained the Spanish-language manuscript for Abad et al. 2013 and had it professionally translated by Languages For Business Ltd. This allowed us to include it in our simplified data analysis, using weighted mean changes/improvements from baseline in various outcome measures.

EAC synthesis and analysis

Due to the lack of transparency in the meta-analysis presented by the Sponsor, the EAC took a more simplified approach to the data presented in the studies. Firstly; the following publications results were combined, as they reported different aspects of the same series of patients:

1) Chin et al. 2012 and Woo et al. 2012 reported urological and sexual function outcomes, respectively, from the same 64-patient case series.

2) Roerhborn et al. 2013 and 2014, and McVary 2014 all report on the LIFT Study RCT. Roehrborn et al. 2013 reports 12 month urological function results, Roerhborn et al. 2014 is a 2-year follow-up report, and McVary reports sexual health outcomes for the initial 12 month follow-up on the LIFT Study.

This was important because some of the results may have been double-counted in the Perera et al. (2014) meta-analysis, if these publications were not combined into their respective studies.

Roerhborn et al. 2014 was provided by the Sponsor alongside their submission of Perera et al. 2014, but not included. Although not a separate study, this does add more long-term data (24-month follow-up) to the LIFT RCT, which the EAC felt was of value to the analysis. Two clinical advisers also requested long-term clinical data, and therefore this publication was included in light of this.

The EAC were asked to provide comparator data for TURP and HoLEP. In order to achieve this, a recent, methodologically-sound systematic review, assessed using a checklist designed by the Support Unit for Research Evidence, Cardiff University (Appendix 3), comparing TURP and HoLEP was sought out (Li et al. 2014). The source publications identified by this review were gathered and relevant outcome data extracted for TURP and HoLEP.

3.9.1 EAC data analysis

Clinically important differences

In order to provide the MTAC Committee with some context to judge the results, the EAC sought out published minimally important differences in each of the reported outcome measures. These are available for questionnaires such as IPSS and IIEF, as they go through a validation and testing process during development.

Where published sources were not available or unsuitable (PVR, for example), the clinical experts were surveyed by the EAC for their opinion on the minimum clinically significant differences in each outcome reported.

Published sources

- IPSS (Barry et al. 1995):
    - Minimum clinically important difference = 3.0 points
    - Moderate difference = 5.1 points
    - Marked difference = 8.8 points
- BPHII (Barry et al. 1995):
    - Minimum clinically important difference = 0.5 points
    - Moderate difference = 1.1 points
    - Marked difference = 2.2 points
- IIEF-5 (Rosen et al. 1999): 4 points.
    - Note: The authors/developers of IIEF-5 (Rosen et al. 1999) classify erectile dysfunction (ED) into five severity grades: no ED (SHIM total score, 22–25), mild (17–21), mild to moderate (12–16), moderate (8–11), and severe ED (1–7). In the published literature, there is no such reported “minimal clinically important difference”. The EAC suggested a minimal difference of four points, as this would carry a patient from one ED classification to another. The majority of clinical experts agreed this was a sensible limit to use for IIEF-5.
- Q_{max} (NICE CG97):
    - Minimum clinically important change = 2ml/s.

- "A consensus during a GDG meeting suggested that a change of 2ml/s is usually considered as important enough to guide treatment decision. The minimal clinical difference was unknown from the patient's perspective."

- PVR is assessed by NICE CG97 as having little value as a measure (or diagnostic indicator) for LUTS because of poor sensitivity and positive/negative likelihood ratios, stating that "elevation of PVR may reflect poor detrusor function as much as obstruction". This was also mentioned to the EAC by one of the specialist clinical advisors. It also does not have questionnaire-style validation, as it is a functional urological measurement.

Table 7 Clinical expert survey for clinical differences

	Expert 1	Expert 2	Expert 3	Expert 4 (drug treatments)	Expert 4 (surgical treatments)
IPSS	3.00	2.50	3	3 to 5	7 to 15
IPSS QoL	1.00		2	1 to 1.5	1.5 to 3
BPHII	2.00			1 to 2	2 to 5
IIEF	3.00		4	6.00	6.00
MSHQ-EjD	1.50				
MSHQ-Bother	1.00				
Qmax (ml/s)	2.50	4.00	5		10-15
PVR (ml)			50		

Blank spaces indicate that a reply was not received, or the expert did not know/was unable to give a clinically significant difference for the outcome measure.

Outcome measures overview – EAC calculations

Table 8 collates all EAC-calculated outcome measures (using weighted means) published studies in the sponsor's submission, as a quick results overview. The outcomes reported are IPSS, IPSS QoL, BPHII, IIEF, MSHQ-EjD, MSHQ-Bother, Qmax and PVR. This is shown for 1, 3, 12 and 24 month follow-up points, as reported. Each individual outcome measure has its own table below that, with individual studies reporting changes from baseline, the number of patients in the study, and significance values (*p*).

Table 8 Overview of EAC-calculated results at 1, 3, 12 and 24 months post-Urolift from baseline (from studies in the Perera et al. (2014) meta-analysis)

	1 month	3 month	12 month	24 month
IPSS (Negative score is improvement)	-10.35	-11.82	-10.49	-9.22
IPSS QoL (Negative score is improvement)	-2.27	-2.48	-2.31	-2.22
BPHII (Negative score is improvement)	-3.29	-3.96	-3.95	-3.76
IIEF (Positive score is improvement)	0.52	1.34	0.80	
MSHQ-EjD (Negative score is improvement)	1.82	1.47	0.83	
MSHQ-Bother (Negative score is improvement)	-0.67	-0.79	-0.91	
Qmax (Positive is improvement)	4.16	3.78	3.52	4.15
PVR (Negative is improvement)	-7.00	-10.34	-5.72	

Outcome measures from all studies

The tables below show mean changes from baseline for each study (Abad et al., 2013; Cantwell et al., 2013; Chin et al. 2012 and Woo et al. 2012 combined cohort study; LIFT combined study results (Roerhborn et al. 2013 and 2014 and McVary 2014), McNicholas et al. 2013; Shore et al. 2014 and Woo et al. 2011), with the number of patients in the analysis, mean results and weighted mean results at 1, 3, 12 and 24 months, where reported.

IPSS score: IPSS scores were widely reported and mean improvements from baseline over 12 months ranged from -9.22 to -11.59 points. All improvements were statistically significant where reported. A higher score is worse, so negative score means a symptom improvement.

Table 9 Mean difference changes in IPSS score in each included study

	IPSS Change from baseline: mean ±SD, (n, *p* value)			
Study	**1 month**	**3 month**	**12 month**	**24 month**
Abad 2013 (no SDs reported for mean change)	-10 (n=20) *p*=0.001)	-9.9 (n=17 *p*<0.001)	-11 (n=9 *p*=0.008)	
Cantwell 2013	-10.9±6.9 (n=53 *p*<0.001)	-11.1±7.2 (n=52 *p*<0.001)	-8.7±7.5 (n=48 *p*<0.001)	
Chin and Woo 2012 (no SDs reported for mean change)		-13.6 (n=62 *p*<0.001)	-10.4 (n=55 *p*<0.001)	
LIFT Study	-9.91±7.08 (n=138 *p*<0.001)	-11.13±7.68 (n=139 *p*<0.001)	-10.63±7.44 (n=126 *p*<0.001)	-9.22±7.57 (n=106 *p*<0.001)
McNicholas 2013 (no SDs reported for mean change)	-10.7 (n=95 *p*<0.001)	-12.6 (n=82 *p*<0.001)	-12.3 (n=51 *p*<0.001)	
Shore 2014	-10.47±7.35 (n=51 *p*<0.001)			
Woo 2011		-11.2±5.7 (n=15 *p*<0.001)	-8.6±7.8 (n=13 *p*=0.002)	
Mean	-10.396	-11.58833333	-10.27166667	-9.22
Weighted mean	-10.3522409	-11.81735695	-10.48701987	-9.22

IPSS QoL: IPSS QoL score mean improvements from baseline ranged from -2.22 to -2.584 points. All improvements were statistically significant where reported. This is to be expected, as QoL is a sub-question of the IPSS, so where IPSS improvement is seen in the table above, there should also be a corresponding QoL improvement. A higher score is worse, so negative score means a symptom improvement.

Table 10 Mean difference changes in IPSS QoL in each included study

	IPSS QoL change from baseline: mean ±SD, (n)			
Study	**1 month**	**3 month**	**12 month**	**24 month**
Abad 2013				
Cantwell 2013	-2.2±1.8 (n=53 *p*<0.001)	-2.3±1.7 (n=52 *p*<0.001)	-2.0±1.7 (n=48 *p*<0.001)	
Chin and Woo 2012 (no SDs reported for mean change)		-2.8 (n=62 *p*<0.001)	-2.4 (n=55 *p*<0.001)	
LIFT Study	-2.01±1.74 (n=138 *p*<0.001)	-2.22±1.78 (n=139 *p*<0.001)	-2.3±1.59 (n=126 *p*<0.001)	-2.22±1.71 (n=106 *p*<0.001)
McNicholas 2013 (no SDs reported for mean change)	-2.9 (n=138 *p*<0.001)	-2.8 (n=65 *p*<0.001)	-2.6 (n=43 *p*<0.001)	
Shore 2014	-2.12±1.94 (n=51 *p*=0.001)			
Woo 2011		-2.8±1.7 (n=15 *p*<0.001)	-2.2±1.9 (n=13 *p*<0.001)	
Mean	-2.3075	-2.584	-2.3	-2.22
Weighted mean	-2.266031746	-2.47981982	-2.30947	-2.22

BPHII: BPHII score mean improvements from baseline ranged from -3.384 to -3.854 points. All improvements were statistically significant where reported. A higher score is worse, so negative score means a symptom improvement.

Table 11 Mean difference changes in BPHII in each included study

	BPHII change from baseline: mean ±SD, (n)			
Study	**1 month**	**3 month**	**12 month**	**24 month**
Abad 2013 (no SDs reported for mean change)	-3.3 (n=20 *p*=0.001)	-3.1 (n=17 *p*=0.001)	-3.4 (n=9 *p*=0.006)	
Cantwell 2013	-3.1±3.3 (n=53 *p*<0.001)	-3.3±2.9 (n=52 *p*<0.001)	-3.1±3.1 (n=48 *p*<0.001)	
Chin and Woo 2012 (no SDs reported for mean change)		-4.6 (n=53 *p*<0.001)	-4.1 (n=46 *p*<0.001)	
LIFT Study	-2.81±3.46 (n=138 *p*<0.001)	-3.96±3.21 (n=139 *p*<0.001)	-3.97±3.26 (n=126 *p*<0.001)	-3.76±3.45 (n=106 *p*<0.001)
McNicholas 2013 (no SDs reported for mean change)	-4.3 (n=68 *p*<0.001)	-4.2 (n=65 *p*<0.001)	-4.7 (n=47 *p*<0.001)	
Shore 2014	-3.41±3.57 (n=51 *p*<0.001)			
Woo 2011				
Mean	-3.384	-3.832	-3.854	-3.76
Weighted mean	-3.28603	-3.961779141	-3.94609	-3.76

IIEF: IIEF score mean changes ranged from +0.483333 to +1.4 points. The majority of changes from baseline were positive, indicating a symptom improvement (a better score indicates better sexual function). However, many of the measurements were not statistically significant, which supports the claim that Urolift does not affect sexual function, and no results indicated a worsening of sexual function post-Urolift.

Table 12 Mean difference changes in IIEF score in each included study

	IIEF change from baseline: mean ±SD, (n)			
Study	**1 month**	**3 month**	**12 month**	**24 month**
Abad 2013				
Cantwell 2013	0.5±4.6 (n=34 *p*=0.51)	0.7±9.2 (n=40 *p*=0.66)	0.9±5.7 (n=33 *p*=0.30)	
Chin and Woo 2012 (no SDs reported for mean change)		2.2 (n=33 *p*=0.004)	1.8 (n=26 *p*=0.01)	
LIFT Study (no SDs reported for mean change)	0.6 (77 *p*=0.309)	1.3 (80 *p*=0.021)	0.4 (73 *p*=0.013)	
McNicholas 2013				
Shore 2014	0.35±4.76 (n=34 *p*=0.67)			
Woo 2011				
Mean	0.483333	1.4	1.033333	
Weighted mean	0.517931	1.337255	0.800758	

MSHQ-EjD: MHSQ-EjD score mean changes ranged from +0.466667 to +1.696667 points. All changes from baseline were positive, indicating a symptom improvement (a higher score indicates better sexual function). Some of the changes from baseline were statistically significant and others were not, however there was only a mean worsening of MHSQ-EjD scores in one time-point of one study (12 month follow-up, Chin and Woo et al. 2012), which does not change the overall mean improvement or weighted mean improvement seen across studies.

Table 13 Mean difference changes in MSHQ-EjD in each included study

	MSHQ-EjD change from baseline: mean ±SD, (n)			
Study	**1 month**	**3 month**	**12 month**	**24 month**
Abad 2013				
Cantwell 2013	1.4±2.3 (n=34 *p*<0.001)	0.3±4.6 (n=39 *p*=0.98)	0.8±2.8 (n=33 *p*=0.62)	
Chin and Woo 2012 (no SDs reported for mean change)		1.6 (n=28 *p*<0.001)	-0.7 (n=22 *p*=0.7)	
LIFT Study (no SDs reported for mean change)	2.1 (n=77 *p*<0.001)	1.8 (n=80 *p*<0.001)	1.3 (n=75 *p*<0.001)	
McNicholas 2013				
Shore 2014	1.59±2.75 (n=34 *p*=0.002)			
Woo 2011				
Mean	1.696667	1.366667	0.466667	
Weighted mean	1.816276	1.470068	0.834615	

MSHQ-Bother: MSHQ-Bother score mean changes from baseline over 12 months ranged from -0.65333 to -0.76667 points. A higher score is worse, so negative score means an improvement. Some of the changes from baseline were statistically significant and others were not. None of the results indicated a worsening of sexual function post-Urolift.

Table 14 Mean difference changes in MSHQ-Bother in each included study

	MSHQ-Bother change from baseline: mean ±SD, (n)			
Study	**1 month**	**3 month**	**12 month**	**24 month**
Abad 2013				
Cantwell 2013	-0.5±1.1 (n=34 *p*=0.008)	-0.4±2.3 (n=37 *p*=0.44)	-0.4±1.4 (n=33 *p*=0.23)	
Chin and Woo 2012 (no SDs reported for mean change)		-0.7 (n=28 *p*<0.001)	-0.7 (n=22 *p*=0.002)	
LIFT Study (no SDs reported for mean change)	-0.7 (n=77 *p*<0.001)	-1 (n=80 *p*<0.001)	-1.2 (n=75 *p*<0.001)	
McNicholas 2013				
Shore 2014	-0.76±1.39 (n=34 *p*=0.003)			
Woo 2011				
Mean	-0.65333	-0.7	-0.76667	
Weighted mean	-0.66717	-0.78897	-0.91231	

Qmax: Qmax mean improvements from baseline ranged from +3.456 to +4.166666667 ml/s. All improvements were statistically significant where reported, with $p<0.05$, so the evidence supports Urolift's ability to increase maximum urine flow rates.

Table 15 Mean difference changes in Qmax in each included study

	Qmax ml/s change from baseline: mean ±SD, (n)			
Study	**1 month**	**3 month**	**12 month**	**24 month**
Abad 2013 (no SDs reported for mean change)	4.5 (n=20 *p*=0.006)	4.8 (n=17 *p*=0.003)	4.2 (n=9 *p*=0.042)	
Cantwell 2013		2.5±5.3 (n=40 *p*=0.002)	2.5±5.0 (n=37 *p*=0.005)	
Chin and Woo 2012 (no SDs reported for mean change)		2.4 (n=46 *p*<0.001)	2.6 (n=39 *p*<0.001)	
LIFT Study		4.24±5.13 (n=124 *p*<0.001)	3.98±4.92 (n=105 *p*<0.001)	4.15±5.05 (n=98 *p*<0.001)
McNicholas 2013 (no SDs reported for mean change)	4.7 (n=67 *p*<0.001)	4.3 (n=80 *p*<0.001)	4 (n=41 *p*<0.001)	
Shore 2014	3.3±4.5 (n=50 *p*<0.001)			
Woo 2011				
Mean	4.166666667	3.648	3.456	4.15
Weighted mean	4.159854015	3.784234528	3.522077922	4.15

PVR: PVR changes from baseline ranged from -3.0575 to -10.55 mls. No changes were statistically significant.

Table 16 Mean difference changes in PVR in each included study

	PVR ml change from baseline: mean ±SD, (n)			
Study	**1 month**	**3 month**	**12 month**	**24 month**
Abad 2013				
Cantwell 2013 (no SDs reported for mean change)		-13.23 (n=51 *p*=0.241)	-11.23 (n=46 *p*=0.262)	
Chin and Woo 2012 (no SDs reported for mean change)		-4 (n=61 *p*=0.7)	8 (n=8 *p*=0.4)	
LIFT Study (no SDs reported for mean change)		-11 (n=137 *p*=0.146)	-12 (n=120 *p*=0.1111)	
McNicholas 2013 (no SDs reported for mean change)	-7 (n=48 *p*=0.775)	-14 (n=41 *p*=0.082)	3 (n=29 *p*=0.299)	
Shore 2014				
Woo 2011				
Mean	-7	-10.55	-3.0575	
Weighted mean	-7	-10.3386	-5.71832	

Note: In order to utilise the results from as many of the studies as possible, results here are not displayed with 95% CIs (This is not done above due to inconsistent reporting of SDs). In Appendix 2 we present these results with 95% CIs.

Comparison with sham control at 3 months (t-test) (from Roerhborn et al. 2013)

The table below is taken from the LIFT Study RCT, comparing Urolift implants to the sham procedure, which involves rigid cystoscopy. This is the only comparative data available for Urolift, and the EAC feels it is of value, as there is a known "sham effect" (Roerhborn et al. 2013) where there is an improvement in IPSS and BPHII after the sham treatment. This is seen below in the "Control ITT group), as there is **some** improvement in these measures. The authors recognise this phenomenon and attribute to a combination of placebo, dilation and regression. However, most importantly, it is only around half of the improvement seen with Urolift; with a statistically significant difference from sham control improvements. Sexual health measures are not significantly different, which supports the Sponsor's claims that Urolift does not affect sexual function in these patients.

Table 17 Intention-to-treat comparison of Urolift and sham control from Roerhborn et al. (2013)

	Urolift-ITT group. Mean±SD (n)			Control ITT group. Mean±SD (n)			
	Baseline	**3 months**	**Change**	**Baseline**	**3 months**	**Change**	***p* Value**
IPSS	22.2±5.48 (140)	11.2± 7.65	-11.1±7.67	24.4±5.75 (66)	18.5±8.59	-5.9±7.66	0.003
IPSS QoL	4.6±1.1 (140)	2.4±1.7	-2.2±1.8	4.7±1.1 (66)	3.6±1.6	-1.0±1.5	0.005
BPHII	6.9±2.8 (140)	3.0±3.1	-3.9±3.2	7.0±3.0 (66)	4.9±3.2	-2.1±3.3	<0.001
IIEF	13.3±8.4 (132)	13.4±9.2	0.1±5.8	13.7±8.5 (65)	15.2±8.5	1.5±6.4	0.139
MSHQ-EjD	8.7±3.1 (94)	10.9±3.2	2.2±2.5	8.8±3.1 (50)	10.5±3.5	1.7±2.6	0.283
MSHQ-Bother	2.4±1.7 (117)	1.6±1.7	-0.8±1.5	2.2±1.7 (60)	1.5±1.7	-0.7±1.6	0.595
Qmax ml/s	8.02±2.43 (126)	12.29±5.4	4.28±5.16	7.93±2.41 (56)	9.91±4.29	1.98±4.88	0.005
PVR ml	85.5±69.2 (140)	75.8±83.9	-9.7±85.5	85.6±70.8 (65)	63.4±64.0	-22.2±70.7	0.306

TURP and HoLEP Comparator data

Note: These "comparative" results must be considered carefully. There are no comparative studies with Urolift vs TURP or HoLEP, and therefore the patient populations may vary and outcome measure improvement e.g. IPSS scores, are highly dependent upon the patients' baseline scores. These numbers are provided by the EAC in order to provide some comparative context to the MTAC committee.

None of the studies in the sponsor's submission are comparative with TURP or HoLEP, as requested in the NICE scope document, and no such studies were identified by the EAC in our independent literature search. Therefore, the EAC performed a rapid pragmatic data synthesis in order to provide some comparative outcome data for these technologies.

The EAC's solution was to find a TURP vs HoLEP systematic review, and extract relevant outcome data from their identified sources. A systematic review search led to the selection of a review by Li et al. 2014, for the following reasons:

- This is a very recent systematic review, published in July 2014, and contains the most recent RCTs – namely a paper by Sun et al., also published in 2014.
- The protocol for this review is published on the PROSPERO website at The University of York Centre for Reviews and Dissemination (CRD) – protocol number CRD42014007334
- Baseline patient characteristics (age, prostate volume, IPSS score and Qmax) are similar to those seen in the Urolift studies in the sponsor's submission:

Table 18 Baselines comparison between Urolift studies and TURp vs HoLEP RCTs from Li et al. (2014)

Outcome measure	Urolift studies	TURP/HoLEP RCTs
Age (years)	64 - 74	65.1 - 72.2
IPSS	21.45 - 26.7	21.9 - 26.4
Prostate volume (mls)	41.3 - 51	36.5 - 77.8
Q_{max} (ml/s)	6.9 – 8.85	4.9 - 8.9

The patient age and IPSS baselines all fall within the same range. The prostate volume range is wider in the TURP/HoLEP RCT studies, particularly skewed slightly towards men with larger prostates. Similarly, the Q_{max} baselines are skewed slightly towards slower flow rates in the baselines of the TURP/HoLEP RCTs.

The EAC critically appraised the systematic review (Li et al. 2014) using a checklist designed by the Support Unit for Research Evidence, Cardiff University.

Results are presented as weighted mean changes from baseline. Negative IPSS, IPSS QoL and PVR results represent an improvement from baseline. Positive Q_{max} results represent an improvement from baseline. The number of studies contributing to the weighted mean results is shown in brackets.

Table 19 Notes on TURP vs HoLEP RCT studies identified by Li et al. (2014)

Study	Notes
Ahyai et al 2007	Replaces Kuntz et al. 2004, as this contains 2-year follow-up results.
Eltabey et al 2010	
Gilling et al 1999	4 year results published, but not usable – dropout rates not reported for each patient group.
Gupta et al 2006	
Mavuduru et al 2009	Only reports results up to 9 months post-procedure.
Montorsi et al 2004	
Sun et al 2014	
Tan et al	2 year and 7 year results published, but not usable – dropout rates not reported for each patient group.

Table 20 EAC-calculated TURP and HoLEP improvements in mean from baselines

TURP	Weighted mean change from baseline (number of studies reporting)			
	1 month	3 month	12 month	24 month
IPSS	-17.34 (5)	-19.70 (2)	-18.13 (7)	-17.50 (1)
IPSS QoL	-2.99 (3)	-2.80 (1)	-3.18 (4)	NR (0)
Q_{max}	14.58 (5)	14.11 (2)	16.69 (7)	23.20 (1)
PVR	-137.43 (3)	-89.34 (1)	-127.29 (3)	-196.10 (1)

HoLEP	Weighted mean change from baseline (number of studies reporting)			
	1 month	3 month	12 month	24 month
IPSS	-17.68 (5)	-20.88 (2)	-19.29 (7)	-20.40 (1)
IPSS QoL	-2.64 (3)	-3.00 (1)	-3.24 (4)	NR (0)
Q_{max}	15.29 (5)	18.25 (2)	17.78 (7)	23.10 (1)
PVR	-160.23 (3)	-78.00 (1)	-161.47 (3)	-231.40 (1)

Notes on these comparative outcome results:

- Both TURP and HoLEP give much better improvement in IPSS scores (including QoL, as these scores are linked) at all time-points:
    - Urolift: -9.22 to -11.82
    - TURP: -17.34 to -19.70
    - HoLEP: -17.68 to -20.88
- Q_{max} improvements are also higher at all time points with both TURP and HoLEP:
    - Urolift: +3.53 to +4.16 ml/s
    - TURP: +14.11 to +23.20 ml/s
    - HoLEP: +15.29 to +23.10 ml/s
- TURP and HoLEP also give better improvements in PVR, but this is less widely reported in both the Urolift studies and the TURP/HoLEP studies. It may be worth noting that one Specialist Clinical Adviser questioned the importance of PVR as an outcome measure for Urolift, and presumably other surgical treatments for BPH

- BPHII scores are not reported in the TURP and HoLEP studies, but as a prostate symptom score, it should give general improvements in agreement with IPSS scores. IPSS is the standard measure of BPH symptom improvement, which may explain the lack of BPHII results with TURP and HoLEP

- Sexual function is poorly reported in the TURP and HoLEP papers (their aim is symptom improvement, so sexual function is secondary, and a complication), and therefore it is difficult to ascertain the impact of these interventions on erectile and ejaculatory function

    - A clinical adviser pointed out that it is difficult to get reliable data on erectile function for the comparator interventions, but recommended the GOLIATH Study (Bachmann et al. 2015) for IIEF-5 reporting post-TURP up to 12 months. GOLIATH patients were measured as **13.7±7.2 at baseline**, and **14.1±8.2 at 12 months post-TURP**, showing no significant changes in a cohort of 119 patients.

    - Two further clinical advisers stated a **5% rate for new erectile dysfunction** and **70-80% retrograde ejaculation rate**, post-TURP.

    - One clinical advisor recommended the 6-year follow-up on HoLEP by Gilling et al. (2008) for sexual function post-HoLEP; and a **76% retrograde ejaculation rate** is reported, which is similar to that quoted by our clinical experts for TURP. IIEF improvement from baseline is not reported.

Complications and procedural data from all Urolift studies

Complications are reported in detail as in all publications. As with outcome data, complications were collated where multiple studies reported on the same patient cohort e.g. the three LIFT study papers. Complications are quantified per study and presented as percentages of total patients, with an overall and 95% CI for each. Complications are grouped according to type: pain and sexual complications, urological, and other (including infections). Procedural data is presented below complications.

Table 21 Urolift complications; pain, haematuria, sexual function

Study	Sample size	Erectile dysfunction		Retrograde ejaculation		Dysuria		Haematuria		Irritative symptoms		Penile pain		Pelvic pain/discomfort		Unspecified pain	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Abad et al. 2013	20	0	0%	0	0%	14	70%	6	30%	8	40%						
Cantwell et al. 2013	53	0	0%	0	0%	20	38%	14	26%					11	21%		
Chin et al. 2012 and Woo et al. 2012	64																
LIFT Study	140	0	0%	0	0%	49	35%	37	26%					27	19%		
McNicholas et al. 2013	102					25	25%	16	16%								
Shore et al. 2014	51					27	53%	38	75%			2	4%	8	16%		
Woo et al. 2011	19	2	11%			11	58%	12	63%	9	47%	1	5%	1	5%	1	5%
Overall (95% CI)			1% (0% to 2%)		0% (0% to 1%)		38% (25% to 51%)		31% (27% to 36%)		44% (29% to 60%)		5% (1% to 11%)		18% (14% to 23%)		5% (1% to 25%)

Table 22 Urolift complications; urological

Study	Sample size	Weak stream		Urinary frequency		Urine flow decreased		Incontinence		Retention		Urgency		Spraying		Incomplete voiding	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Abad et al. 2013	20									2	10%						
Cantwell et al. 2013	53							2	4%	4	8%	7	13%				
Chin et al. 2012 and Woo et al. 2012	64																
LIFT Study	140							6	4%	1	1%	13	9%				
McNicholas et al. 2013	102									3	3%	10	10%				
Shore et al. 2014	51			0	0%	0	0%	2	4%	3	6%	4	8%				
Woo et al. 2011	19	1	5%					3	16%	3	16%			2	11%	1	5%
Overall (95% CI)			5% (1% to 25%)		0% (0 to 7%)		0% (0 to 7%)		5% (3% to 8%)		4% (2% to 6%)		10% (7% to 4%)		11% (3% to 31%)		5% (1% to 25%)

Table 23 Urolift complications; other

Study	Sample size	Bladder spasm		Prostatitis		Orchitis/ epidiymitis		Urinary tract infection		Rigor	
		n	%	n	%	n	%	n	%	n	%
Abad et al. 2013	20					1	5%				
Cantwell et al. 2013	53	3	6%								
Chin et al. 2012 and Woo et al. 2012	64			1	2%	1	2%	7	11%	1	2%
LIFT Study	140	6	4%					4	3%		
McNicholas et al. 2013	102					3	3%	3	3%		
Shore et al. 2014	51										
Woo et al. 2011	19	3	16%	1	5%			1	5%		
Overall (95% CI)			6% (3% to 9%)		4% (1% to 10%)		3% (1% to 6%)		5% (3% to 7%)		2% (0% to 8%)

Table 24 Urolift complications; procedural data

Study	Sample size	Reoperation rate		Procedure time (mins)		Local anaesthesia		Return to normal activity (days)		Catheter required		Catheter duration (hrs) [1]		Encrusted implants		Encrusted implants removed	
		n	%	mean	SD	n	%	mean	SD	n	%	mean	SD	n	%	n	%
Abad et al. 2013	20	1	5%	19.1		0	0%			2	10%			0	0%		
Cantwell et al. 2013	53	1	2%	53	15.0	46	87%	6.5	6.8	26	49%	33					
Chin et al. 2012 and Woo et al. 2012	64	13	20%							34	53%	20		0	0%		
LIFT Study	140	11	8%	66.2	23.8	139	99%	8.6	7.5	40	29%	21.6		10	7%	6	4%
McNicholas et al. 2013	102	4	4%	57.8	15.8					54	53%						
Shore et al. 2014	51			52	22.0	50	98%	5.1	5.8	10	20%	16					
Woo et al. 2011	19	3	16%							13	68%			0	0%		
Overall (95% CI)			8% (5% to 11%)	59.6 (57.5-61.7)	20.2		93% (89% to 96%)	7.4 (6.7-8.2)	5.9		39% (35% to 44%)	22.3			3% (1% to 6%)		4% (2% to 9%)

[1]Catheter duration was not always reported with SDs, so 95% CIs could not be calculated.

Length of stay data was only reported by Abad et al. 2013, at 2.6 hrs (range 3-72). Otherwise, Shore et al. report "All patients were treated as day cases, there were no overnight stays", but this is not quantifiable.

It is also worth noting the 100% general anaesthesia use by Abad et al. in their protocol, and the markedly shorter procedure time. This may be a facet of having a patient under general anaesthetic, but the publication does not clarify this. However, the shorter procedure time in the Abad et al. (2013) study does not impact the weighted mean greatly due to the low patient number in this case series. The EAC asked clinical advisers about Urolift procedure times, and many said that it could be done in 30 minutes (from their own practical experience), and that 60 minutes was under "trial conditions".

Complications and procedural data from all TURP vs HoLEP studies

Table 25 TURP complications; pain, haematuria, sexual function

Study	Sample size	Dysuria		Irritative symptoms	
		n	%	n	%
Ahyai et al 2007	88				
Eltabey et al 2010	40			8	20%
Gilling et al 1999	59				
Gupta et al 2006	50	1	2%		
Mavuduru et al 2009	15	3	20%		
Montorsi et al 2004	48	13	27%		
Sun et al 2014	82				
Tan et al 2003	30				
Overall (95% CI)			13% (0% to 36%)		20% (10% to 35%)

Table 26 TURP complications; urological

Study	Sample size	Incontinence		Retention	
		n	%	n	%
Ahyai et al 2007	100	1	1%		
Eltabey et al 2010	40	12	30%		
Gilling et al 1999	59	1	2%		
Gupta et al 2006	50				
Mavuduru et al 2009	15	0	0%		
Montorsi et al 2004	48	18	38%	1	2%
Sun et al 2014	82				
Tan et al 2003	30	11	37%		
Overall (95% CI)			11% (0% to 30%)		2% (0% to 11%)

Table 27 TURP complications; other

Study	Sample size	Urinary tract infection		Transfusion		TUR Syndrome		Bladder neck contracture		Urethral stricture		BPH recurrence	
		n	%	n	%	n	%	n	%	n	%	n	%
Ahyai et al 2007	100			2	2%			3	3%	3	3%	0	0%
Eltabey et al 2010	40			3	8%					2	5%		
Gilling et al 1999	59			4	7%					6	10%		
Gupta et al 2006	50			1	2%	1	2%			2	4%		
Mavuduru et al 2009	15			1	7%								
Montorsi et al 2004	48					1	2%			4	8%		
Sun et al 2014	82				11%		21%			4	5%		
Tan et al 2003	30	2	7%	1	3%					2	7%		
Overall (95% CI)			7% (2% to 21%)		6% (4% to 8%)		9% (0% to 24%)		3 (1% to 8%)		6% (4% to 9%)	0% (0% to 4%)	

Table 28 TURP complications; procedural data

Study	Sample size	Reoperation rate		Procedure time (mins)		Length of stay (hrs)		Catheter required		Catheter duration (hrs)	
		n	%	mean	SD	mean	SD	n	%	mean	SD
Ahyai et al 2007	100	7	7%	73.8	24.00	85.8	39.10	5	5%	43.4	21.10
Eltabey et al 2010	40			73.6	22.30	91.2	38.40			50.4	26.40
Gilling et al 1999	59	4	7%			47.5	17.37	8	14%	37.2	15.92
Gupta et al 2006	50			64.1	13.10			3	6%	45.7	12.70
Mavuduru et al 2009	15			43	9.36			1	7%	78.2	17.84
Montorsi et al 2004	48	1	2%	57	15.00	85.8	18.90			57.78	17.50
Sun et al 2014	82			62.91	27.52	283.68	81.84			127.43	75.93
Tan et al 2003	30	2	7%			49.9	5.60	4	13%	44.9	5.60
Overall (95% CI)			6% (4% to 10%)	65.9	16.4	122.3	47.2		8% (5% to 12%)	62.7	37.4

Table 29 HoLEP complications; pain, haematuria, sexual function

Study	Sample size	Dysuria		Irritative symptoms	
		n	%	n	%
Ahyai et al 2007	100				
Eltabey et al 2010	40			10	25%
Gilling et al 1999	61				
Gupta et al 2006	50	5	10%		
Mavuduru et al 2009	15	1	7%		
Montorsi et al 2004	52	33	63%		
Sun et al 2014	82				
Tan et al 2003	30				
Overall (95% CI)			31% (0% to 80%)		25% (14% to 40%)

Table 30 HoLEP complications; urological

Study	Sample size	Incontinence		Retention	
		n	%	n	%
Ahyai et al 2007	100	1	1%		
Eltabey et al 2010	40	8	20%		
Gilling et al 1999	61				
Gupta et al 2006	50	1	2%		
Mavuduru et al 2009	15	2	13%		
Montorsi et al 2004	52	26	50%	3	6%
Sun et al 2014	82				
Tan et al 2003	30	15	50%		
Overall (95% CI)			14% (0% to 38%)		2% (0% to 11%)

Table 31 HoLEP complications; Other

Study	Sample size	Urinary tract infection		Transfusion		TUR Syndrome		Bladder neck contracture		Urethral stricture		BPH recurrence	
		n	%	n	%	n	%	n	%	n	%	n	%
Ahyai et al 2007	100							3	3%	4	4%	1	1%
Eltabey et al 2010	40			0	0%					1	3%		
Gilling et al 1999	61	3	5%	0	0%					6	10%		
Gupta et al 2006	50			0	0%					1	2%		
Mavuduru et al 2009	15												
Montorsi et al 2004	52					0	0%			1	2%		
Sun et al 2014	82				1%		6%			3	4%		
Tan et al 2003	30	0	0%	0	0%					1	3%		
Overall (95% CI)			3% (0% to 8%)		1% (0% to 2%)		3% (0% to 12%)		3% (1% to 8%)		4% (3% to 7%)		1% (0% to 5%

Table 32 HoLEP complications; procedural data

Study	Sample size	Reoperation rate		Procedure time (mins)		Length of stay (hrs)		Catheter required		Catheter duration (hrs)	
		n	%	mean	SD	mean	SD	n	%	mean	SD
Ahyai et al 2007	100		7%	94.6	35.10	53.3	15.90	0	0%	27.6	10.40
Eltabey et al 2010	40			72.8	21.70	62.4	28.80			36	33.60
Gilling et al 1999	61	1	2%			26.1	11.71	5	8%	20	11.39
Gupta et al 2006	50			75.4	22.80			2	4%	28.6	20.50
Mavuduru et al 2009	15			53	9.84			1	7%	46.42	14.25
Montorsi et al 2004	52	1	2%	74	19.50	59	19.90			31	13.00
Sun et al 2014	82			70.17	29.51	272.88	94.32			113.63	50.61
Tan et al 2003	30	0	0%			27.6	2.70	5	17%	17.7	2.70
Overall (95% CI)			4% (2% to 7%)	72.1	20.5	97.8	47.4		4% (0% to 11%)	44.2	26.8

Notes on complications comparison between Urolift, TURP and HoLEP studies

As with the clinical outcome measures being compared earlier, these results should be interpreted cautiously and in knowledge that there are no true comparative studies between Urolift and TURP or HoLEP. One weakness of this type of comparative approach is that the Urolift studies report a different set of complications than those reported for TURP vs HoLEP RCTs, and with good reason: Urolift complications seem to be typically mild, such as transient dysuria or haematuria. Presumably, dysuria and haematuria are expected occurrences with TURP and HoLEP. Therefore, these are not as widely reported in the TURP vs HoLEP RCTs, in part due to them being so normal and their mild nature. Similarly, implant encrustation is not an event that can occur with TURP or HoLEP, but where seen, the implants can easily be removed with forceps without further issue. This was largely supported by when the EAC asked the clinical advisers, and the majority did not see implant encrustation as a significant issue.

Other complications comparisons (of those most widely reported):

- Incontinence was less prevalent with Urolift (5%, CI 3% to 8%) compared to TURP (11%, CI 0% to 30%) and HoLEP (14%, CI 0% to 38%)
- Reoperation rates were slightly higher with Urolift (8%, CI 5 % to 11%) compared to TURP 4% (2% to 7%) and HoLEP (6%, CI 4% to 10%)
- Procedure time is shorter with Urolift (59.6 mins ± 20.2) compared to TURP (72.1 mins ± 20.5) and HoLEP (65.9 mins ± 16.4). The EAC asked clinical advisers about the Urolift procedure time, in their experience. The majority said that the procedure could be done in 30 minutes, and that 60 minutes was under “trial conditions”.

Additional notes:

- Length of stay was poorly reported in the Urolift studies, which means a comparison cannot be made to TURP and HoLEP. The EAC asked clinical advisers about the Urolift length of stay, and the majority said that it was done as a daycase procedure, with very few patients needing an overnight stay.

- Erectile function, urinary tract infection, prostatitis, orchitis and bladder spasm were poorly reported in the TURP vs HoLEP RCTs, which means a comparison cannot be made to Urolift. The EAC asked the clinical experts about this:
    - One clinical adviser pointed out that it is difficult to get reliable data on erectile function for the comparator interventions, but recommended the GOLIATH Study (Bachmann et al. 2015) for IIEF-5 reporting post-TURP up to 12 months. GOLIATH patients showed no significant changes in IIEF-5 post-TURP.
    - Two further clinical advisers stated a **5% rate for new erectile dysfunction** and **70-80% retrograde ejaculation rate**, post-TURP.
    - Another clinical advisor recommended the 6-year follow-up on HoLEP by Gilling et al. (2008) for sexual function post-HoLEP; and a **76% retrograde ejaculation rate** was reported, which is similar to that quoted by our clinical experts for TURP. IIEF improvement from baseline is not reported.
- Catheterisation rates vary due to local procedures (e.g. some hospitals seem to catheterise post-procedurally as a matter of course) so this is a difficult comparison to make. Post-procedure catheterisation times were shorter for Urolift (22.3 hrs, no SDs reported) compared to TURP (62.7 hours ± 37.4) and HoLEP (44.2 hours ± 26.8). However, this again could be decided by local procedures rather than patient need, or a genuine difference between the surgical procedures.

The mild complications of the Urolift procedure may be enough to for some patients, concerned about blood loss or TUR syndrome, to prefer Urolift if it was offered to them as an alternative to TURP and HoLEP by their urologist.

3.10 Conclusions on the clinical evidence

The sponsor's submission uses pooled effect sizes to show mean changes from baseline in a number of key areas: prostate symptom score measures (IPSS, BPHII), health-related quality of life (IPSS QoL), male sexual health (IIEF, MSHQ-EjD, MSHQ-Bother) and urological function (Q_{max} and PVR) up to 12-months post-Urolift. The presented meta-analysis indicates a large improvement in prostate symptom scores and QoL, a small improvement (but not negative

impact) on sexual health. The authors note that Q_{max} and PVR were inconsistently reported, leading to a higher heterogeneity score in their meta-analysis, which made true effects difficult to assess.

The EAC considers that this meta-analysis does show that Urolift is clinically effective, but is not a clear representation of the data. The methodology in the systematic review paper was short and lacked transparency, certain patients from some of the publications could have been double-counted (multiple publications covered some of the cohorts involved, but again, this is not clearly stated in the methods) and effect sizes are less clear than simply using the units of the outcome measures themselves. The EAC attempted to address this in our analysis by maintaining the original units of the outcome measures of each study, rather than converting to effect sizes, and taking a more simplified approach of reporting the mean change from baseline in each outcome measure reported.

Overall, the studies used in the sponsor's submission show that Urolift is a clinically effective device for the treatment of BPH. However, this relies upon context. Using the IPSS score as a primary outcome for symptom improvement, the published minimally important change in IPSS score is 3 (Barry et al. 2005), and Urolift delivers a weighted mean IPSS improvement of between 9.22 – 11.82 points. These Urolift improvements are also larger than the published "marked improvement" in IPSS score of 8.8 (Barry et al. 1995). Therefore, in light of the published evidence on the IPSS tool, Urolift delivers very satisfactory clinical results.

However, the EAC comparison using papers selected by a recent TURP vs. HoLEP systematic review (Li et al. 2014) showed that patients with a similar range of baselines (age, IPSS score, prostate volume, Q_{max}) made much better improvements in IPSS with both TURP and HoLEP. A similar effect is seen in IPSS QoL, Q_{max}, and PVR: although improvements are made with Urolift, all symptom-related measures improve more dramatically with both TURP and HoLEP.

Sexual function is poorly reported in the TURP and HoLEP RCTs (the study aims are mostly based around symptom improvement, so sexual function impact is secondary outcome, and a complication), and therefore it is difficult to ascertain the impact of these interventions on erectile and ejaculatory function. The evidence shows that Urolift does not negatively affect

these outcomes, but small improvements are achieved, however these are not always statistically significant.

The mild complications of the Urolift procedure (mainly dysuria and haematuria) may be of interest to some patients, specifically those wishing to avoid blood loss or TUR syndrome. These were either not reported as a complication of Urolift, or are not possible with Urolift, respectively. Furthermore, the clinical improvements of IPSS (discussed above) may also be enough to satisfy patients with severe BPH, as a 10 point improvement would carry a patient from “severe BPH” (20-35 points) to “moderate BPH” (8-19 points) (British Association of Urological Surgeons).

Therefore, the evidence may support Urolift being used an alternative, based upon patient preference, for symptom relief lower than that of TURP or HoLEP, but at reduced risk of the more dangerous complications.

Table 33 Overview of outcome measures

	Published or clinical expert opinion – minimally important change	Urolift	TURP	HoLEP
IPSS (Negative score is improvement)	Minimum = 3.0 Moderate = 5.1 Marked change = 8.8 (Barry et al. 1995)	1 month -10.35 3 month -11.82 12 month -10.49 24 month -9.22	1 month -17.34 3 month -19.70 12 month -18.13 24 month -17.50	1 month -17.68 3 month -20.88 12 month -19.29 24 month -20.40
IPSS QoL (Negative score is improvement)	Minimum = 1-3 (Clinical expert opinion)	1 month -2.27 3 month -2.48 12 month -2.31 24 month -2.22	1 month -2.99 3 month -2.80 12 month -3.18 24 month N/A	1 month -2.64 3 month -3.00 12 month -3.24 24 month N/A
BPHII (Negative score is improvement)	Minimum = 0.5 Moderate = 1.1 Marked changed = 2.2 (Barry et al. 1995)	1 month -3.29 3 month -3.96 12 month -3.95 24 month -3.76	N/A	N/A
IIEF (Positive score is improvement)	Minimum = 4 (Clinical expert opinion)	1 month +0.52 3 month +1.34 12 month +0.80 24 month N/A	N/A	N/A
MSHQ-EjD (Negative score is improvement)	Minimum = 1.5 (Clinical expert opinion)	1 month +1.82 3 month +1.47 12 month +0.83 24 month N/A	N/A	N/A
MSHQ-Bother (Negative score is improvement)	Minimum = 1.0 (Clinical expert opinion)	1 month -0.67 3 month -0.79 12 month -0.91 24 month N/A	N/A	N/A
Qmax (ml/s) (Positive is improvement)	Minimum = 2ml/s (NICE CG97)	1 month +4.16 3 month +3.78 12 month +3.52 24 month +4.15	1 month +14.58 3 month +14.11 12 month +16.69 24 month +23.20	1 month +15.29 3 month +18.25 12 month +17.78 24 month +23.10
PVR (ml) (Negative is improvement)	Minimum = 50 ml (Clinical expert opinion)	1 month -7.00 3 month -10.34 12 month -5.72 24 month N/A	1 month -137.43 3 month -89.34 12 month -127.29 24 month -196.10	1 month -160.23 3 month -78.00 12 month -161.47 24 month -231.40

4 Economic evidence

4.1 Published economic evidence

4.1.1 Critique of the sponsor's search strategy

The sponsor has combined the search for relevant economic studies with a search for evidence to inform model inputs. Therefore the search is broader than the PICO in the scope, for example including studies that evaluate interventions/procedures other than Urolift. The search terms used were:

(Benign prostatic hyperplasia OR benign prostatic enlargement) AND Cost

The use of 'AND cost' is overly restrictive, since some studies may include other terms such as economic, or variations on this. The clinical terms are also restrictive and more terms should have been included, such as LUTS and variations on this.

NHS EED was searched for economic evidence. The NHS EED database is populated by a search of CINAHL, Embase, MEDLINE, PsycINFO and PubMed, which already incorporates an economic filter, therefore there was no need to include 'AND cost'. If possible a search of EconLit would have made the search for evidence more thorough. The sponsor's submission also included a search of the manufacturer's internal literature databases and reference list checking of all relevant study publications. The search for evidence did not include citation tracking of included studies or contacting authors of the included studies

Grey literature was searched using Google and there was a search of the NICE website.

The EAC conducted a search in the following databases: Cost Effectiveness Analysis; EcoLit; HEED and NHS EED for economic evidence concerning Urolift. This was in addition to the searches for clinical evidence described in 3.1, which would have also identified economic evidence. The EAC search identified 40 citations.

4.1.2 Critique of the sponsors study selection

The sponsor provided a flow chart to describe the study selection process. Studies were excluded if they:

- Did not take a UK perspective
- Did not look solely at BPH
- Were focused on specific sub-groups
- Evaluated non-BPH treatments

4.1.2 Included and excluded studies

None of the studies included by the sponsor included Urolift. They were all economic studies of the comparators, including comparators in the scope and others outside the scope. Therefore none of the studies are appropriate for inclusion, although some may include useful data for inputs to the model regarding the comparators.

The EAC conducted a thorough search for economic studies relevant to the scope, described in 4.1. No relevant economic studies were identified.

4.1.3 Overview of methodologies of all included economic studies

N/A

4.1.4 Overview and critique of the sponsor's critical appraisal for each study

The sponsor carried out a critical appraisal for each economic study, but as these were not relevant to the scope, this was not required.

4.1.5 Does the sponsor's review of economic evidence draw conclusions from the data available?

The sponsor noted that 'no cost-effectiveness analysis comparing these technologies in the NHS is currently available' and this is the rationale for the de novo model.

4.2 De novo cost analysis

Patients

The population considered in the model is men with LUTS secondary to BPH aged ≥ 50 years, and with prostate volume no greater than 100cc. This accords with the population in the scope.

Technology

The technology in the model is Urolift, in accordance with the scope. The results for Urolift are presented alongside the comparators.

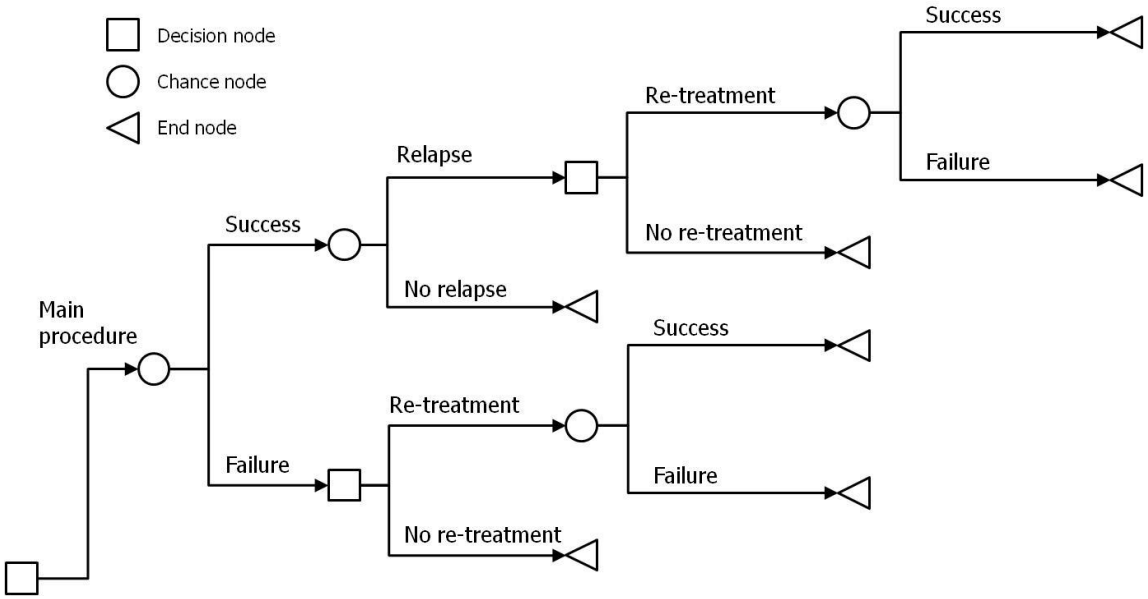
Comparator(s)

In the model the sponsor included TURP and HOLEP as comparators in agreement with the scope. The executable model also included Bipolar TURP, laser vapourisation (e.g. KTP laser) TUVP, and Bipolar TUVP as comparator arms but in the sponsor submission only the comparators in the scope are presented.

Model structure

The model structure is a decision tree, with seven executable arms, one for each technology or comparator. Following treatment the outcomes are success or failure. The success category then has options for relapse or no relapse. The relapse option then has success or failure outcomes. The failure outcome has options for re-treatment (with success or failure outcomes) or no re-treatment.

Figure 2 Flow diagram of sponsor's de novo economic model



There are three possible perspectives to be selected in the executable model:

1. Hospital (1 year timeframe)
2. Primary Care Trust (1 year timeframe)
3. National (NHS) 2 year time horizon

The sponsor submission refers only to the NHS perspective and 2 year time horizon. The two year time horizon was chosen to be long enough to assess the majority of differences in outcomes, treatment related adverse events and re-interventions. It is also the maximum length of follow-up available in the published evidence for Urolift.

The overall structure of the model is cumbersome because of the inclusion of comparators outside the scope, pre-operative and post-operative tests which are the same regardless of the intervention and options for additional perspectives not referred to in the submission.

The model includes detailed costing for complications. For example, incontinence includes the costs of drugs, incontinence bags and pads and nurse visits. The costs are taken from reliable sources.

Model assumptions

The sponsor provided a comprehensive list of 21 assumptions in the model together with a justification for each. The list is reproduced below in Table 35, together with EAC comments.

Table 34 Model assumptions

Assumption	Justification	EAC comment
The initial procedure is either successful or not. Failure is defined as failure to achieve ≥10% improvement in IPSS score relative to baseline within 30 days of procedure	In clinical practice a percentage change of less than 10% in IPSS is most often used to define insufficient improvement (Lourenco 2008)	Accept
In the base case, the proportion of patients who decide to undergo retreatment is the same for patients who have failed the initial treatment, and patients who had an initially successful procedure but then experience relapse		Accept
The mean IPSS score post treatment of patients who have failed is the same as the mean IPSS score pre-treatment, i.e. there is no change in mean IPSS score for failed patients:		Accept

The probability of retreatment after failure is equal to the probability of retreatment after relapse. I.e. patients with an unsatisfactory treatment result after the initial procedure have the same probability of retreatment regardless of the reason (initial failure, or subsequent relapse after a successful result)		Accept
The success rate for subsequent procedures is lower than for primary procedures. The relative success of a subsequent procedure compared to a primary procedure is assumed to be 0.75.	This value was used in the model was estimated from clinical expert opinion (Lourenco 2008).	Accept. Agrees with NICE CG97.
In the base case, retreatment is carried out using TURP for all patients except for those who have HoLEP as the initial procedure, for whom there is no surgical option	TURP represents the 'gold standard' of surgical treatments for BPH. Patients who have undergone a HoLEP procedure would not be eligible for further surgical treatment due to the enucleation of tissue in the prostate.	Accept
The operation time for UroLift is assumed to be 30 minutes	Assumption based on clinical expert opinion	Based on weighted mean in studies, EAC considers 60 minutes is the best available published data. This should be explored in sensitivity analysis.
The operation time for TURP is assumed to be 60 minutes	Assumption based on clinical expert opinion	Weighted mean of published studies is 66 minutes.
The operation time for HoLEP is assumed to be 76.96 minutes	Calculated as the summation of operating time by TURP and the weighted mean difference obtained from a meta-analysis (Lourenco 2008)	77 minutes is used in the sponsor's model
The operation time for HoLEP is assumed to be 58.38 minutes	Calculated as the summation of operating time by TURP and the weighted mean difference obtained from a meta-analysis (Lourenco 2008)	I think this refers to KTP laser rather than HoLEP
Length of hospital stay = 0.5 days for UroLift	Assumption based on clinical expert opinion	EAC clinical experts consider Urolift to be a day case procedure.
Length of hospital stay = 3.03 days for TURP	Weighted average of HRG4 codes LB25A, LB25B, LB25C (HSCIC 2013)	EAC weighted mean = 5.08 days However this includes a study with unusually high number of TUR syndrome cases. Accept sponsor value.
Length of hospital stay = 1.98 days for HoLEP	Calculated as the summation of operating time by TURP and the weighted mean difference obtained from the meta-analysis (Lourenco 2008)	EAC weighted mean = 4.08 days. However this includes one study with an unusually long LOS. Accept sponsor value.
Length of hospital stay = 2.33 days for Bipolar TURP	Calculated as the summation of operating time by TURP and the weighted mean difference obtained from the meta-analysis ((Lourenco 2008)	Accept
The total capital costs of equipment for TURP = 0.	It was assumed that equipment for TURP is already available in the NHS	EAC includes a capital cost of £10 per patient for TURP equipment
No. of cystoscopy sets used per procedure =1	Clinical expert opinion	Accept
The number of pre- and post-operative tests and healthcare visits does not differ between any of the surgical interventions	Clinical expert opinion	Agree but the sponsor claimed 'significantly lower number of post discharge follow-on visits' for Urolift. One clinical expert agreed that complications were lower with Urolift than TURP/HoLEP so fewer post-procedure visits needed. One clinical expert stated that more post-procedure visits were needed in the short term because Urolift is new and lacks data.

Each treatment is associated with the same levels of operating staff (1 consultant surgeon, Consultant anaesthetist, 1 band 5 nurse and 1 healthcare assistant	Clinical expert opinion	Clinical advisers suggested an additional laser operator is needed for HoLEP.
For all procedures excluding UroLift, there is risk of permanent incontinence	The risk of incontinence from each procedure were derived from the identified from meta-analyses (Lourenco 2008). For UroLift no cases of permanent incontinence post-procedure have been reported for any patient receiving the procedure to date. Clinicians also indicated that the procedure was very safe and had no effect on incontinence	Accept
Mortality is excluded from the model	There is no evidence to suggest that treatments for BPH influence overall survival. Hence, due to the short time horizon of the model, mortality was excluded from the model.	Agree
Costs were discounted at 3.5%	This is the rate recommended by NICE technology evaluation programme (NICE 2011)	Agree

The EAC did not identify any additional model assumptions.

Clinical parameters and variables

Data sources used for clinical parameters for Urolift were the papers by Lourenco 2008, Chin 2012 and Woo 2011 and unpublished data from Roehrborn 2014.

Table 35 Probability of success per procedure (>10% improvement in IPSS within 12 months)

UroLift	TURP	HoLEP	Bi-TURP
89.08%	94.00%	96.71%	94.00%

Table 36 Probability of relapse after successful procedure (long term)

UroLift	TURP	HoLEP	Bi-TURP
0.00%	0.17%	0.32%	0.99%

The probability of relapse for Urolift after successful procedure (long term) is based on limited data since only one study extended to 2 years and all other studies stopped at 12 months post procedure. Therefore it is difficult to be confident that there is zero chance of relapse. The EAC has looked at the effect of increasing the probability to 0.2% on the results of the model, and this increases the cost of Urolift by £4.

Table 37 Probability of re-treatment within 31 days (short term)

UroLift	TURP	HoLEP	Bi-TURP
0.75%	0.31%	0.21%	0.45%

Table 38 Probability of adverse effects per procedure (%)

	UroLift	TURP	HoLEP	Bi-TURP
Incontinence	0.00%	3.00%	2.91%	1.77%
Urinary retention	5.71%	5.00%	3.55%	8.55%
UTI	1.40%	6.00%	5.88%	6.00%
Stricture	0.00%	7.00%	5.88%	9.66%
TUR syndrome	0.00%	3.00%	0.93%	3.00%
Decrease in erectile function	0.00%	9.15%	9.06%	9.15%
Increase in erectile function	0.00%	3.42%	4.32%	3.42%
Ejaculation dysfunction	0.00%	37.45%	33.44%	37.45%

The EAC found the weighted mean for incontinence to be 5% (CI 3% to 8%), but this included stress and urgency incontinence. No permanent incontinence was reported for Urolift, therefore the EAC accepts the sponsor value.

The EAC calculates UTIs as 5% (CI 3% to 7%) for Urolift from the published studies, which is actually higher than claimed and similar to comparators. Considering that the operation time is similar, sterility of components is the same; we might expect similar UTI rates. Perhaps the lack of irrigation in Urolift could reduce the UTI rate.

The model doesn't specifically include:

- 3% (CI 1% to 10%) prostatitis
- 3% (CI 1% to 6%) orchitis/epididymitis

It is possible that these are included in UTI in the model, but these are not clearly reported in the published literature.

The EAC considered the erectile and ejaculatory function for Urolift is fine at 0%. There was actually a small mean improvement in IIEF (although not statistically significant), for example.

Procedural variables in the model including hospital LOS (0.5 days) and procedure time (30 minutes) for Urolift were based on clinical opinion of three experts. Procedure time was quite well reported in the literature, and the EAC calculated weighted mean was 59.6 minutes. One paper (Abad 2013) reported a 19 minute procedure time under general

anaesthetic, but this was a small study and all of the other studies showed close agreement for a procedure time with a range from 52-66 minutes.

None of the studies reported LOS for Urolift, therefore it is reasonable to use expert opinion to inform the base case. However, the sensitivity analysis needs to be across a broad range of values as there is considerable uncertainty around this estimate. LOS could be longer than 0.5 days, particularly since patients are reported to be catheterised for a weighted mean of 22.3 hours (this assumes that patients were not sent home with catheters *in situ*).

The EAC consulted clinical experts regarding LOS and operative time for Urolift. The responses were varied, but the majority classed Urolift as a true day case procedure. One adviser commented that the operative time in the published literature (59.6 minutes) may reflect trial conditions and that practical experience confirmed a 30 minute procedure time was normal.

Resource identification, measurement and valuation

The number of Urolift devices is a key driver of the model and in the base case the sponsor has used 4 as the number of devices per procedure. The reference given for this value is Chin 2012 and in the executable model it states this was also validated by clinical experts. The EAC agrees that Chin 2012 reported the mean number of devices per procedure to be 4, but published studies reported using between 2 and 9 devices per procedure. The EAC calculated the weighted mean number of implants from all of the clinical studies and found this to be 4.4 devices per procedure. We suggest that this is a more representative value for this parameter.

The cost of blood transfusion has been overestimated by the sponsor as £862.17 per transfusion. The data source (NICE CG97) references Varney and Guest (2003) and in this paper the authors conducted a top down cost analysis of transfusion services. It was assumed that a transfusion would increase LOS by 1 day and this was included in the cost of transfusion (£635 in 2003 inflated by the sponsor to current value of £826.17). The LOS for the comparators in the model is based on data from Lourenco (2008) and would include any

increase in LOS for blood transfusion. Therefore the sponsor is double counting 1 extra day LOS for patients having blood transfusion. The EAC estimates the cost of blood transfusion as £329. 1 unit standard red cells = £ 121.85 (NHS Blood and Transplant price list 2014/15. The mean number of units per transfusion is estimated to be 2.7 units of red blood cells (Varney and Guest 2003). Therefore the EAC calculates 2.7 x £121.85 = £329 per transfusion.

Although blood transfusion only occurs in 8% of patients undergoing TURP and fewer patients having HoLEP procedure (relative risk for HoLEP compared with TURP = 0.27), the probability of blood transfusion for Urolift in the model is 0, therefore this change reduces the cost of the comparators, but not Urolift.

The unit cost of hospital stay has been taken from published Scottish data for Urology specialty in-patient costs, divided by the average length of stay (3.3 days) to give the unit cost per day in hospital. The excess bed day cost used in the model is calculated from the HRG code for TURP, minus the procedure costs included in the model. It is not very clear which procedure costs have been subtracted. The result is £331 in 2012 prices which is inflated to £344 current price. The cost used in the model for hospital stay (0.5 days) for Urolift is calculated from 0.5 x £344 = £172. For comparison the EAC found the cost of an excess bed-day from the National Schedule of reference costs 2013-14 to be £294 (Excess bed day LB25F).

Technology and comparators' costs

The list price of Urolift implants is given as £330 excluding VAT per device by the sponsor.

Table 39 Consumables included in the sponsor's model

	Details	Cost per procedure	EAC comment
Urolift	4 implants @ £330	£1320	This is the largest component in the cost of Urolift.
mTURP	1 loop electrode @ £52.50	£52.50	Assume use of 1 loop electrode & 1 roller/ball in 100% of cases. Based upon NHS Supply Chain list of diathermy equipment costs: Covidien E7506 Diathermy plate standard (solid) with leadwire = £4.04 Loop electrode (models suitable for mTURP = £26.40 Roller/ball electrode (models suitable for mTURP = £26.40 Total = £56.84
HoLEP	Reusable fibre @ £614.37 (20 uses) Reusable morcellator @ £664.63 (10 uses)	£97.18	EAC investigated single use fibre @ £368.61 from NHS supply chain
Bi-TURP	1 loop electrode @ £52.50	£52.50	Change to £56.84 as above

The sponsor includes in the model the option to not re-use the HoLEP consumables, but there is no adjustment in the price of these. Selecting this option increases the cost of HoLEP from £1924 per procedure to £3106, making Urolift cost saving compared with HoLEP. The EAC considers that single use consumables would be offered at a lower price than multi-use consumables. It is unlikely that hospitals would dispose of multi-use consumables after a single use, so we consider this option unrealistic. The EAC looked at the result of using single use laser fibres @ £368.61 from NHS supply chain catalogue price, but we retained the re-usable morcellator blade as we did not find a cost for these from NHS supply chain or a manufacturer.

Table 40 Capital costs of equipment used in the sponsor's model

	Capital cost (assumed lifespan of equipment of 10 years, and used for 250 patients/year)	Cost per procedure
Urolift	£5199	£2.50
mTURP	£0	£0
HoLEP	£167,555	£80.60
Bi-TURP	£0	£0

There is an option in the model to replace the purchase of the capital equipment with a contract for a number of consumables over a time period. If this option is selected for Urolift the capital cost of the equipment (£5199) is excluded from the model. However nothing else changes in the model, so selecting this option for Urolift has the effect of simply subtracting £2.50 from the cost per patient of the procedure. Therefore it has minimal effect on the outcome of the model. For HoLEP where the capital equipment costs are significant (£167,555), choosing this option has the effect of reducing the cost of HoLEP from £1924 to £1843 per patient, the difference being £81, which is the cost per procedure of the capital equipment. The EAC considers it likely that manufacturers would charge a higher price per consumable item if such a contract were agreed in order to recoup the capital cost of the equipment. The EAC consulted clinical advisers about this, but we were unable to obtain specific details of negotiated contracts, which may vary between manufacturers and NHS organisations.

Sensitivity analysis

Since the base case shows Urolift to be more costly than the comparators, sensitivity analysis is of great importance. The sponsor has identified the key drivers in the model based on the sensitivity analysis. For Urolift the model is driven by the cost of the device and the number of devices used for each patient.

The results of sensitivity analysis were not saved in the executable version of the model, so it was necessary to change each parameter in turn, run the model and record the results.

For parameters investigated in sensitivity analysis the upper and lower values used were ±20% of base case values. This is reasonable when the variable is known with some certainty, but where the parameter is based on opinion of a small number of clinicians or on poor quality data, it would be more robust to allow the parameters to take a wider range.

Hospital length of stay was not identified as a key driver for Urolift in the model, but as there was no published data on LOS for Urolift, the sponsor relied on clinical opinion (3 clinicians) for the estimate of 0.5 days. Sensitivity analysis considered this variable, and it was varied by ±20%, so the range considered was 0.4 days to 0.6 days.

For the length of operation, which is estimated to be 30 minutes for Urolift it would be helpful to see a more robust sensitivity analysis, rather than a standard ±20% variation.

In the sensitivity analysis the sponsor has assumed in the base case that the HoLEP consumables (laser fibre and morcellator) are re-used 20 and 10 times respectively. An additional scenario was analysed in which reuse of HoLEP consumables was not permitted. The EAC found that NHS supply chain offer both single use and reusable laser fibres for HoLEP, and the reusable fibres are more expensive. For example Cook Medical multi-use fibres cost £1207.42 each, but their single use fibres cost £368.61. The sponsor has used the same price for single use and multi-use fibres and morcellators. Based on the source of the data these appear to be multi-use fibres. The sponsor appears to suggest that hospitals are disposing of multi-use consumables after a single use and the EAC considers this to be an unlikely scenario.

4.3 Results of de novo cost analysis

Base-case analysis results

The sponsor's base case results are shown in Table 9.2.5 taken from the sponsor's submission and this matches the results in the executable model. The sponsor also presented the incremental costs for Urolift (Table 9.2.6 in the sponsor's submission) . The EAC has combined these tables below, in T able 41.

Table 41 Sponsor's base case results

Intervention	Total cost per patient	Incremental cost of Urolift
UroLift	£2 342	-
TURP	£2 339	+£3
HoLEP	£1 924	+£ 418
Bipolar TURP	£2 302	+£40

The threshold at which Urolift becomes cost neutral compared with mTURP is reached when each Urolift device falls in price from £330 to £329. The sponsor also included a breakdown of costs by category reproduced below in Table 27. It is evident from this table that Urolift has much greater equipment costs per procedure than the comparators, but lower clinical supplies and services costs due to the estimated shorter length of hospital stay.

Table 42 Sponsor's breakdown of costs

Item	UroLift	TURP	HoLEP	Bi-TURP
Medical [1]	£342	£423	£457	£410
Nursing	£64	£113	£137	£105
Drugs[2]	£22	£21	£20	£21
Clinical supplies and services [3]	£549	£1,358	£923	£1,222
Equipment cost per procedure	£1,325	£56	£97	£56
Other[4]	£40	£369	£290	£487
TOTAL	£2,342	£2,339	£1,924	£2,302
[1]Consultant staff costs, [2]Cost of anaesthetic doses, saline, and antibiotics, [3]Includes cost of tests pre- and post- procedure and hospital bed day costs, [4]Includes costs of complications and capital costs				

Sensitivity analysis results

The results of sensitivity analysis are not presented very clearly by the sponsor and so the EAC has calculated the results of sensitivity analysis undertaken by the sponsor and these are presented in Table 43 below.

Table 43 Results of sponsor's sensitivity analysis

Parameter		UroLift	TURP	HoLEP	Bi-TURP
Base case		**£2342**	**£2339**	**£1924**	**£2302**
UroLift device cost per procedure	+20%	£2606			
	-20%	£2078			
12 month failure probability	+20%	£2389	£2362	£1926	£2322
	-20%	£2295	£2319	£1922	£2282
Duration of operation	+20%	£2373	£2404	£2003	£2359
	-20%	£2311	£2274	£1845	£2239
Length of stay	+20%	£2376	£2560	£2061	£2432
	-20%	£2308	£2120	£1786	£2044

Other parameters tested in sensitivity analysis are listed in Table 44 below. These had a uniformly small impact on the model (less than 1%) for all procedures.

Table 44 Other parameters tested in the sponsor's sensitivity analysis

Probability of incontinence after TURP
Probability of blood transfusion after TURP
Probability of urinary retention
Probability of UTI
Probability of stricture
Probability of TUR syndrome after TURP

Subgroup analysis

No subgroup analysis was undertaken by the sponsor. A sub-group of interest identified in the scope was ‘Men for whom TURP or HoLEP is unsuitable because of difficulties with

blood loss or sedation'. No evidence was found for this sub-group on which to base a model scenario.

Model validation

The sponsor states that the model was subject to internal quality checking. No published studies comparing Urolift with TURP or HoLEP were found, therefore the model could not be validated against any published results. The sponsor noted that in respect of the comparators, the results were consistent with published models, showing HoLEP is less costly than TURP.

4.4 Interpretation of economic evidence

The sponsor cites the lack of comparative efficacy data between Urolift and TURP or HoLEP as a weakness of the submission. The sponsor identifies a resource saving of 27 minutes of operating room time. In the model the reduction in operating time only included a reduction in staff time. There was no cost of the operating theatre included. The EAC have accounted for this in section 4.5, Table 48 Effect of adding theatre overhead costs to the sponsor's model.

4.5 Additional work undertaken by the External Assessment Centre in relation to economic evidence

The EAC sought to verify the sponsor's estimate for length of hospital stay for Urolift patients with clinical advisers. There was some variation in the responses, but all confirmed that the Urolift procedure can be considered day case, and that length of stay would be measured in hours rather than days. All EAC changes to the model were also accompanied by threshold analysis, where the cost per Urolift implant could be altered to allow Urolift to become cost neutral compared to mTURP.

Based on the weighted mean of studies reporting the number of Urolift implants used per procedure, the EAC substituted the sponsor's estimate of 4 with the weighted mean of 4.4. This had the effect of increasing the cost of Urolift by £132. The threshold analysis at which Urolift achieves cost neutrality with mTURP under these conditions is £299 per implant.

Table 45 Effect of changing the number of Urolift implants

Model input		Values	Urolift	mTURP	HoLEP	BiTURP
No of Urolift implants	Sponsor	4	£2342	£2339	£1924	£2302
	EAC	4.4	£2474	£2339	£1924	£2302

The EAC changed the sponsor's estimate of 30 minutes for the operation time for Urolift to 60 minutes based on the weighted mean of reported operation time from published studies. This had the effect of increasing the cost of Urolift by £154. The threshold analysis at which Urolift achieves cost neutrality with TURP under these conditions is £291 per implant.

Table 46 Effect of changing the procedure time for Urolift

Model input		Values	Urolift	mTURP	HoLEP	BiTURP
Operation time for Urolift	Sponsor	30 minutes	£2342	£2339	£1924	£2302
	EAC	60 minutes	£2496	£2339	£1924	£2302

The EAC changed the mTURP procedure time from the sponsor's 60 minutes to the weighted mean of 66 minutes taken from the EAC comparator studies. This increased the cost of mTURP so that Urolift became cost saving, by £26 per patient. Threshold analysis shows that Urolift implants would cost £337 each in order to make them cost neutral with mTURP.

Table 47 Effect of changing the procedure time for mTURP

Model input		Values	Urolift	mTURP	HoLEP	BiTURP
Operation time for mTURP	Sponsor	60 minutes	£2342	£2339	£1924	£2302
	EAC	66 minutes	£2345	£2371	£1924	£2302

The sponsor claims that Urolift can save 27 minutes of operating theatre time, but the EAC could not find operating theatre time cost accounted for in the model. We took the cost of a urology operating theatre from NICE CG97, stated at £9 per minute. For an hour's operation this is £540. We inflated this to 2015 values and then subtracted the staff costs from the sponsor's model, leaving an operating theatre overhead cost of £314 (£5.23 per minute). We validated this by comparison with another economic analysis by Noble et al. (2002), who give an inflation-adjusted cost for urological theatre time of £280 per hour (separate from staff costs). There is nowhere in the model to include theatre overheads, but we used £314 per hour as a theatre overhead cost, and inserted £5.23 per minute into the line titled "Band 5 nurse (second)" in the sponsor's economic model. This gives a per-minute cost to account for the theatre time in the model. This produces a cost saving of £139 compared to mTURP and £79 compared to BiTURP.

Table 48 Effect of adding theatre overhead costs to the sponsor's model

Model input		Values	Urolift (30 mins)	mTURP (60 mins)	HoLEP (76.96 mins)	BiTURP (55.44 mins)
Theatre overheads	Sponsor	£0	£2342	£2339	£1924	£2302
	EAC	£5.23 per minute	£2532	£2671	£2372	£2611

Some clinical experts advised that TURP may need an extra band 5 nurse over Urolift to handle irrigation fluid, so the EAC changed this. This was done for mTURP and BiTURP. These staffing changes made Urolift cost saving over mTURP, by £78, and BiTURP by £34.

Table 49 Effect of adding an additional band 5 nurse to mTURP and BiTURP

Model input		Values	Urolift	mTURP	HoLEP	BiTURP
Band 5 nurse	Sponsor	1 band 5 nurse	£2342	£2339	£1924	£2302
	EAC	2 band 5 nurses	£2351	£2429	£1924	£2385

The EAC changed the cost of blood transfusion in the model from £862.17 which includes double counting of 1 additional day in hospital to the EAC estimate of £329. This had the effect of reducing the cost of the comparators such that Urolift costs £44 more than mTURP, compared with £3 more in the base case. Threshold analysis shows that under these new conditions, Urolift implants would have to be priced at £319 per implant to achieve cost neutrality with mTURP.

Table 50 Effect of changing the blood transfusion cost

Model input		Values	Urolift	mTURP	HoLEP	BiTURP
Cost of transfusion	Sponsor	£862.17	£2342	£2339	£1924	£2302
	EAC	£329	£2338	£2294	£1913	£2255

The EAC included a £10 per procedure cost for capital equipment for TURP (total capital cost £20,799 used both mTURP and biTURP) as the sponsor did not include the capital cost in the base case. This had the effect of increasing the cost of the TURP comparators such that Urolift became cost saving compared with mTURP by £7 per patient.

Table 51 Effect of including the capital equipment costs for TURP

Model input		Values	Urolift	mTURP	HoLEP	BiTURP
Cost of mTURP and BiTURP capital equipment	Sponsor	£0	£2342	£2339	£1924	£2302
	EAC	£10	£2343	£2349	£1924	£2312

mTURP procedures use a roller or ball electrode in addition to the loop electrode in up to 100% of cases. mTURP also requires a return electrode plate. The EAC found costs for these electrodes from NHS supply chain catalogue. Our total consumables cost for mTURP comes to £56.84, which is slightly higher than the cost used by the sponsor. The effect on the model is to make Urolift cost neutral compared to mTURP. This was also done for BiTURP consumables, but did not make Urolift cost saving when compared to BiTURP

Table 52 Effect of changing the cost of mTURP and BiTURP consumables

Model input		Values	Urolift	mTURP	HoLEP	BiTURP
Cost of mTURP consumables	Sponsor	£52.50	£2342	£2339	£1924	£2302
	EAC	£56.84	£2343	£2343	£1924	£2306

The HoLEP fibres are priced differently when they are single-use. In light of this, the EAC took a price of £368.61 for single-use HoLEP fibres from NHS Supply Chain, and limited them to single use in the sponsor's model. Under these conditions, Urolift was still cost incurring compared to HoLEP, by £80 per patient.

.Note: The EAC were unable to find a cost for single-use morcellator blades (either through Supply Chain or by contacting a manufacturer, Lumenis (Versacut)) and this means they may not be available or widely used. Therefore, we retained the sponsor's original figures for re-useable morcellator blades.

Table 53 Effect of changing the HoLEP fibres to single-use

Model input		Values	Urolift	mTURP	HoLEP	BiTURP
HoLEP fibres	Sponsor	£614.27, 20 uses	£2342	£2339	£1924	£2302
	EAC	£368.61, single use	£2342	£2339	£2262	£2302

Some clinical experts advised that HoLEP may need an extra band 5 nurse as a laser operator, so the EAC changed this. Urolift was still cost incurring compared to HoLEP under these conditions, by £309 per patient. Urolift becomes cost saving with this change when the price of the Urolift implants falls to £252 each.

Table 54 Effect of adding an additional band 5 nurse (laser operator) to HoLEP

Model input		Values	Urolift	mTURP	HoLEP	BiTURP
Band 5 nurse	Sponsor	1 band 5 nurse	£2342	£2339	£1924	£2302
	EAC	2 band 5 nurses for HoLEP	£2342	£2339	£2033	£2302

When all EAC changes are incorporated in the model simultaneously, Urolift is cost incurring compared with all other options.

Table 55 Effect of all EAC changes to the model

Model input	Urolift	mTURP	HoLEP	BiTURP
Base case	£2342	£2339	£1924	£2302
All EAC changes	£2979	£2707	£2762	£2579
Incremental cost of Urolift (negative if Urolift is cost saving)		£272	£217	£400

Threshold analysis for all the EAC conditions shows that each Urolift implant would have to cost £268 in order to achieve cost neutrality with mTURP.

There is remaining uncertainty in the LOS for Urolift which is based on clinical opinion. The EAC has contacted clinical advisers and there is consensus that Urolift is a truly day case procedure. The sponsor sensitivity analysis considered LOS in the range 0.4 to 0.6 days. The EAC considers this too narrow and looked at the range 0.25 to 1 days LOS. At 0.25 days, Urolift is cost saving against mTURP by £83, and threshold analysis gives a Urolift implant cost of £351 per implant. At 1 day's LOS, Urolift is cost incurring compared to mTURP by £175, and threshold analysis shows that cost neutrality would require a cost of £286 per implant.

Table 56 EAC sensitivity analysis on LOS

Model input		Urolift	mTURP	HoLEP	BiTURP
Base case LOS	0.5 days	£2342	£2339	£1924	£2302
Urolift LOS EAC sensitivity	0.25 days	£2256			
	1 day	£2514			

The cost of a bed-day used in the model is based on an in-patient stay. The definition of day surgery in the UK is that 'the patient must be admitted and discharged on the same day, with day surgery as the intended management'. Several patients per day may be admitted to the same trolley space in a dedicated day unit, providing greater efficiency than can be achieved for a day case in a general ward (AAGBI Day Case and Short Stay Surgery Guideline 2011). Therefore, the actual length of stay for Urolift procedures is of great importance in a dedicated day surgery unit.

We were also able to perform sensitivity analysis for reusable HoLEP fibres, at a cost of £1207.42 (NHS Supply Chain). This was used as an upper-limit sensitivity analysis for this input. Table 57 below shows that even at this increased cost, the high number of uses for these fibres means that it makes very little impact on the cost of HoLEP.

Table 57 EAC sensitivity analysis for reusable HoLEP fibres

Model input		Values	Urolift	mTURP	HoLEP	BiTURP
HoLEP fibres	Sponsor	£614.27, 20 uses	£2342	£2339	£1924	£2302
	EAC	£1207.42, 20 uses	£2342	£2339	£1954	£2302

The model includes an option via a drop-down list to select Urolift performed under local anaesthetic. However, when selected there is no change in the result of the model and the EAC determined that this element of the model is not functioning.

4.5.1 EAC scenario

Based on responses from clinical advisers to EAC questions the EAC has identified an optimistic but realistic scenario in which Urolift is cost saving compared with mTURP. In our scenario, we see the Urolift procedure undertaken within a dedicated day surgery unit.

Table 58 EAC scenario inputs and conditions

Input	Conditions	Source/notes
Length of stay	0.125 days (3 hrs)	Clinical expert advice
Urolift procedure time	30 mins	Clinical expert advice/sponsor's model
Number of Urolift implants	4*	Sponsor's model
Local anaesthetic used for Urolift procedure	Remove consultant anaesthetist cost from model	Clinical expert advice
Theatre overhead cost	5.23 per minute	Added to model as Nurse Band 5 (second)
mTURP procedure time	66 mins	EAC weighted mean from clinical section of this Assessment Report
Cost of blood transfusion	£329	EAC figure (sponsor's original input was too high)

Table 59 EAC scenario cost results

	Urolift	mTURP	HoLEP	BiTURP
Sponsor base case	£2342	£2339	£1924	£2302
EAC scenario	£2355	£2691	£2315	£2564
Incremental cost of Urolift (negative if Urolift is cost saving)		-£336	£40	-£209

In the scenario, Urolift is cost saving by £336 compared with mTURP and by £209 compared with BiTURP.

*if the EAC figure of 4.4 Urolift implants is used (which accounts for the range of implant numbers required, reported as 2-9 in the Urolift studies), Urolift is still cost saving compared to mTURP and BiTURP under these conditions.

4.6 Conclusions on the economic evidence

The sponsor's submission relies on a de novo cost model. The model is comprehensive and somewhat overly complex as it includes pre- and post-procedure elements that are the same for the intervention and all comparators. The executable model also includes comparators not in the scope. The model options produce scenarios that the EAC considers unrealistic, such as the option for removing the capital equipment costs, but not changing the cost of consumables.

The major limitation of the model is that the base case shows that Urolift is not cost saving against any of the comparators, although it is close to cost neutral compared with mTURP (+£3). There are limited opportunities to improve this position because the cost per procedure for Urolift is strongly driven by the large cost per procedure of the implants. The costs of the comparators are strongly driven by LOS, which is well reported in the literature. The EAC has made changes to the model, some of which are in favour of Urolift, but the overall effect of EAC changes is to worsen the position of Urolift compared with mTURP and BiTURP.

Remaining uncertainties concern the LOS for Urolift, which is 0.5 days in the base case and is based on clinical opinion. The sensitivity analysis only considers a narrow range from 0.4 days to 0.6 days. The EAC has increased this range from 0.25 days to 1 day because of the uncertainty in the value. If the LOS were 0.25 days, the cost per procedure for Urolift changes from £2342 to £2256, and Urolift becomes cost saving against mTURP and BiTURP. If the LOS for Urolift is increased to 1 day, the cost per procedure for Urolift increases to £2514 per procedure and Urolift remains the most costly of the interventions and comparators. After consulting clinical advisers regarding the LOS for Urolift, the EAC devised a scenario for Urolift undertaken in a dedicated day surgery unit, which was cost saving for Urolift compared with mTURP, with a £336 compared with mTURP and by £209 compared with BiTURP.

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4.6.1 Impact on the cost difference between the technology and comparator of additional clinical and economic analyses undertaken by the External Assessment Centre

The impact of the EAC changes on the results of the model are summarised in Table 39 below. Shaded rows of the table are results when Urolift becomes cost saving.

Table 60 Impact of EAC changes on the model

	Urolift	mTURP	HoLEP	BiTURP
Sponsor base case	£2342	£2339	£1924	£2302
No of Urolift implants = 4.4	£2474	£2339	£1924	£2302
Operation time for Urolift = 60 minutes	£2496	£2339	£1924	£2302
Operation time for mTURP = 66 minutes	£2345	£2371	£1924	£2302
Addition of urological theatre overhead costs	£2532	£2671	£2372	£2611
Cost of transfusion = £329	£2338	£2294	£1913	£2255
Cost of mTURP and BiTURP capital equipment per patient = £10	£2343	£2349	£1924	£2312
Cost of TURP consumables = £56.84	£2343	£2343	£1924	£2306
HoLEP fibres single use @ £368.61	£2342	£2339	£2262	£2302
Additional band 5 nurse for HoLEP	£2342	£2339	£2033	£2302
All above changes	£2979	£2707	£2762	£2579
EAC scenario	**£2355**	**£2691**	**£2315**	**£2564**

If all EAC changes are incorporated in the model, Urolift becomes cost saving compared with mTURP when the price for each Urolift device falls to £268.

Urolift becomes cost saving compared with mTURP in the following circumstances, accepting the sponsor model, and making any one of the following changes only:

- Increasing the operation time for mTURP from 60 to 66 minutes
- Including the capital cost of equipment for mTURP £10 per patient
- Decreasing the LOS for Urolift from 0.5 days to 0.25 days

- One additional band 5 nurse for mTURP
- Including operating theatre overheads
- The cost of a Urolift implant decreases from £330 to below £329

Urolift becomes cost saving compared with BiTURP in the following circumstances, accepting the sponsor model and making any one of the following changes:

- Decreasing the LOS for Urolift from 0.5 days to 0.25 days
- Including operating theatre overheads
- Additional band 5 nurse for BiTURP
- The cost of a Urolift implant decreases from £330 to below £320

Urolift becomes cost saving compared with HoLEP in the following circumstances, accepting the sponsor model and making one change:

- The cost of a Urolift implant decreases from £330 to £225 or below

5 Conclusions

Overall, the studies used in the sponsor's submission show that Urolift is a clinically effective device for the treatment of BPH, giving IPSS score improvements from baseline greater than that deemed a "marked improvement" by the original developers of the IPSS score (Barry et al. 1995). However, the scope of this assessment called for comparative studies with Urolift versus TURP or HoLEP, and none such publications currently exist. In order to provide comparative context, the EAC used before-and-after data from papers selected by a recent TURP vs. HoLEP systematic review (Li et al. 2014). This pragmatic comparison shows that Urolift is out-performed by TURP and HoLEP in terms of IPSS, QoL and Qmax improvements from baseline, in patients with similar baseline characteristics.

However, Urolift appears to have the advantage in terms of minimal and mild complications, and this may be of great interest to certain patients and urologists. The clinical evidence shows that Urolift is associated with slight improvements in sexual function, and although not statistically significant, it certainly does not adversely affect these outcomes. The EAC's comparative exercise for TURP and HoLEP show that sexual function is not well reported in

many TURP and HoLEP RCTs (their main focus is IPSS and urological improvements), and this led to consultation of the clinical experts. The experts agreed on a 5% erectile dysfunction rate and 70-80% retrograde ejaculation rate post-TURP and HoLEP. The most serious of the TURP and HoLEP-related complications, are either not possible with Urolift (TUR syndrome) or not a risk due to the nature of the Urolift procedure (blood transfusion). The evidence may support Urolift being used an alternative, based upon patient preference, for symptom relief lower than that of TURP or HoLEP, but at reduced risk of the more dangerous complications.

The economic case for Urolift was made using a very detailed and thorough de novo cost model. Inputs to the model were well-researched and relied upon a robust HTA for TURP and HoLEP comparator and cost data (Laurenco et al. 2008) as well as Urolift outcome data from the LIFT Study. The model also had a lot of irrelevant data, such as results for TUVP, which was outside of the NICE scope for this assessment.

The base case posed by the sponsor placed Urolift at almost cost-neutral (£3 cost incurring) compared to TURP and £418 cost incurring compared to HoLEP. Sensitivity analysis showed that the key drivers of the model were the cost of the Urolift device and length of stay post-procedure. It was difficult to overcome the initial cost of the Urolift implants, even with the length of stay and complications savings made post-procedure. The EAC identified a number of conditions which changed the sponsor's model result for Urolift from cost incurring to cost saving for each comparator. Against HoLEP, Urolift was only cost saving if the price of the Urolift implants was reduced to less than £225.

The EAC present a scenario in which Urolift can be cost-saving compared to TURP, but not HoLEP. This relies upon a low number of Urolift implants, a short procedure time of 30 minutes or less, adding urological operating theatre overhead costs, local anaesthetic, and a day-case procedure of 0.125 days (3 hours). Under these conditions, savings of £336 compared with mTURP and £209 compared with BiTURP are achievable. All of the inputs of the EAC scenario are supported by published sources or by clinical experts for the assessment, who are currently using the Urolift device in the UK.

6 Implications for research

There is currently no published data directly comparing Urolift with TURP or HoLEP, as specified in the scope of this assessment. The logical response would be to suggest a truly comparative, preferably randomised, two- armed trial with at least one of these comparator technologies, or a three-armed trial with both TURP and HoLEP as comparators. This would ensure a single, defined patient population and eliminate baseline characteristics differences. Collecting resource use data as part of this trial would also strengthen the economic data available for decision makers regarding Urolift.

The BPH-6 trial, currently active but not recruiting, will go some way to addressing this research need. Although it only uses TURP as a comparator to Urolift, TURP is the most common surgical treatment for BPH in the UK, so this is arguably the most important comparison to make. The EAC contacted the sponsor and one of the PIs for BPH-6 (who is also a clinical expert for this assessment) and were assured that preliminary data from this study would be available in March 2015. It may be possible to update this report, or supply an additional data sheet, when these results become available.

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Appendix

Appendix 1: EAC literature search strategies

Example: Ovid MEDLINE(R) search

1) Prostatic Hyperplasia/
2) Urethral obstruction/ or urinary bladder neck obstruction/
3) Lower Urinary Tract Symptoms
4) LUTS.tw
5) (urin* adj3 tract* adj3 (sympt* or block*)).tw
6) ((urin* or urethra*) adj3 (obstruct* or block*)).tw
7) (Prostat* adj3 Hyperplas*).tw
8) (prostat* adj3 hypertroph*).tw
9) (prostat* adj3 adenoma*).tw
10) Prostatism/
11) Prostatism.tw
12) or/1-11
13) urolift.tw
14) Urologic Surgical Procedures, Male/
15) (urethra* adj3 lift*).tw
16) Prostat* adj3 lift*.tw
17) or/13-16
18) 12 and 17
19) Animals/ not humans/ exp animals/ not humans.sh.
20) 18 not 19

All other database searches were adaptations of the above.

Appendix 2: Urolift results with 95% CIs

The EAC-calculated weighted means for outcome measure results are shown in section 3.9.1 (Table 7 –Table 15). Below we present 95% CIs alongside weighted means, although it is only possible to present 95% CIs where SDs are reported. Due to inconsistent reporting of SDs in the studies, there are far fewer studies included than in the main results presented by the EAC in section 3.9.1. These results were calculated using RevMan v5.3 using the general inverse variance option. The confidence intervals account for heterogeneity, where significant, using a random effects analysis.

IPSS

	IPSS change from baseline 1 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
Cantwell 2013	53	-10.9	6.9	-10.90 [-12.76, -9.04]
LIFT Study	138	-9.91	7.08	-9.91 [-11.09, -8.73]
Shore 2014	51	-10.47	7.35	-10.47 [-12.49, -8.45]
Total				-10.25 [-11.14, -9.36]

	IPSS change from baseline 3 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
Cantwell 2013	52	-11.1	7.2	-11.10 [-13.06, -9.14]
LIFT Study	139	-11.13	7.68	-11.13 [-12.41, -9.85]
Woo 2011	15	-11.2	5.7	-11.20 [-14.08, -8.32]
Total				-11.13 [-12.13, -10.13]

	IPSS change from baseline 12 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
Cantwell 2013	48	-8.7	7.5	-8.70 [-10.82, -6.58]
LIFT Study	126	-10.63	7.44	-10.63 [-11.93, -9.33]
Woo 2011	13	-8.6	7.8	-8.60 [-12.84, -4.36]
Total				-9.80 [-11.23, -8.37]

	IPSS change from baseline 24 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
LIFT Study	106	-9.22	7.57	-9.22 [-10.66, -7.78]

IPSS QoL

	IPSS QoL change from baseline 1 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
Cantwell 2013	53	-2.2	1.8	-2.20 [-2.68, -1.72]
LIFT Study	138	-2.01	1.74	-2.01 [-2.30, -1.72]
Shore 2014	51	-2.12	1.94	-2.12 [-2.65, -1.59]
Total				-2.07 [-2.30, -1.85]

	IPSS QoL change from baseline 3 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
Cantwell 2013	52	-2.3	1.7	-2.30 [-2.76, -1.84]
LIFT Study	139	-2.22	1.78	-2.22 [-2.52, -1.92]
Woo 2011	15	-2.8	1.7	-2.80 [-3.66, -1.94]
Total				-2.29 [-2.53, -2.05]

	IPSS QoL change from baseline 12 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
Cantwell 2013	48	-2	1.7	-2.00 [-2.48, -1.52]
LIFT Study	126	-2.3	1.59	-2.30 [-2.58, -2.02]
Woo 2011	13	-2.2	1.9	-2.20 [-3.23, -1.17]
Total				-2.22 [-2.46, -1.99]

	IPSS QoL change from baseline 24 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
LIFT Study	106	-2.22	1.71	-2.22 [-2.55, -1.89]
Total				-2.22 [-2.55, -1.89]

BPHII

	BPHII change from baseline 1 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
Cantwell 2013	53	-3.1	3.3	-3.10 [-3.99, -2.21]
LIFT Study	138	-2.81	3.46	-2.81 [-3.39, -2.23]
Shore 2014	51	-3.41	3.57	-3.41 [-4.39, -2.43]
Total				-3.00 [-3.43, -2.56]

	BPHII change from baseline 3 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
Cantwell 2013	52	-3.3	2.9	-3.30 [-4.09, -2.51]
LIFT Study	139	-3.96	3.21	-3.96 [-4.49, -3.43]
Total				-3.70 [-4.33, -3.06]

	BPHII change from baseline 12 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
Cantwell 2013	48	-3.1	3.1	-3.10 [-3.98, -2.22]
LIFT Study	126	-3.97	3.26	-3.97 [-4.54, -3.40]
Total				-3.60 [-4.44, -2.76]

	BPHII change from baseline 24 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
LIFT Study	106	-3.76	3.45	-3.76 [-4.42, -3.10]
Total				-3.76 [-4.42, -3.10]

IIEF

	IIEF change from baseline 1 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
Cantwell 2013	34	0.5	4.6	0.50 [-1.05, 2.05]
Shore 2014	34	0.35	4.76	0.35 [-1.25, 1.95]
Total				0.43 [-0.68, 1.54]

	IIEF change from baseline 3 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
Cantwell 2013	40	0.7	9.2	0.70 [-2.15, 3.55]
Total				0.70 [-2.15, 3.55]

	IIEF change from baseline 12 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
Cantwell 2013	33	0.9	5.7	0.90 [-1.04, 2.84]
Total				0.90 [-1.04, 2.84]

MSHQ-EjD

	MSHQ-EjD change from baseline 1 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
Cantwell 2013	34	1.4	2.3	1.40 [0.63, 2.17]
Shore 2014	34	1.59	2.75	1.59 [0.67, 2.51]
Total				1.48 [0.89, 2.07]

	MSHQ-EjD change from baseline 3 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
Cantwell 2013	39	0.7	4.6	0.70 [-0.74, 2.14]
Total				0.70 [-0.74, 2.14]

	MSHQ-EjD change from baseline 12 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
Cantwell 2013	33	0.8	2.8	0.80 [-0.16, 1.76]
Total				0.80 [-0.16, 1.76]

MSHQ-Bother

	MSHQ-Bother change from baseline 1 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
Cantwell 2013	34	-0.5	1.1	-0.50 [-0.87, -0.13]
Shore 2014	34	-0.76	1.39	-0.76 [-1.23, -0.29]
Total				-0.60 [-0.89, -0.31]

	MSHQ-Bother change from baseline 3 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
Cantwell 2013	37	-0.4	2.3	-0.40 [-1.14, 0.34]
Total				-0.40 [-1.14, 0.34]

	MSHQ-Bother change from baseline 12 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
Cantwell 2013	33	-0.4	1.4	-0.40 [-0.88, 0.08]
Total				-0.40 [-0.88, 0.08]

Qmax

	Qmax change from baseline 1 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
Shore 2014	50	3.3	4.5	3.30 [2.05, 4.55]
Total				3.30 [2.05, 4.55]

	Qmax change from baseline 3 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
Cantwell 2013	40	2.5	5.3	2.50 [0.86, 4.14]
LIFT Study	124	4.24	5.13	4.24 [3.34, 5.14]
Total				3.51 [1.83, 5.19]

	Qmax change from baseline 12 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
Cantwell 2013	37	2.5	5	2.50 [0.89, 4.11]
LIFT Study	105	3.98	4.92	3.98 [3.04, 4.92]
Total				3.39 [1.97, 4.81]

	Qmax change from baseline 24 month			
Study	**n**	**Mean**	**SD**	**Mean (95% CI)**
LIFT Study	98	4.15	5.05	4.15 [3.15, 5.15]
Total				4.15 [3.15, 5.15]

PVR

No SDs reported for PVR results, therefore it was not possible to calculate 95% CIs.

Appendix 3: Critical appraisal of Li et al. (2014)

Support Unit for Research Evidence (SURE) Questions to assist with the critical appraisal of a systematic review[1]

Citation: Li 2014 Registered on Prospero http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42014007334

Questions ** relate to whether the methodology used is described – eg independently in duplicate

1. Does the review address a clearly focused question/hypothesis	Yes	Can't tell	No
Population/Problem?	Yes		
Intervention?	Yes		
Comparator/control?	Yes		
Outcomes? Can you identify the primary outcome?	Yes		
2. Did the authors look for the appropriate types of paper? Did the studies address the review's question and have an appropriate design?	Yes		
3. Is the search likely to have identified all the relevant evidence?	Yes generally ok but no search for clinical trials or manufacturer contact		

Sufficient range of databases searched? Date range appropriate?	
Good range of search terms (indexed terms and keywords)	
Reference list/bibliography checking?	
Hand search (journals)	
Grey literature searched (unpublished work) Websites? Contacting experts/manufacturers?	
Search terms/ strategy provided? Were they comprehensive?	
Search results provided (no of hits and final studies)? Flow diagram?	
All languages included?	
4. Are all relevant studies likely to have been included?	Yes
Are the inclusion and exclusion criteria stated?	
Is the study selection process described? **	
Multiple papers relating to same study identified?	
Is the data extraction process described? **	
5. Did the authors assess the quality (rigour) of the included studies?	Yes
Is the assessment process described? **	
6. Information about included studies Is key information provided (eg study design, population, interventions, comparators, outcomes,	Yes

areas of potential bias)?	
7. If the results of the review have been combined (meta-analysis), was this appropriate?	Yes
Were the studies sufficiently similar in design and results?	
Are the reasons for any variations discussed?	
8. Are results provided for all included studies? Do the conclusions reflect all results? Is the quality assessment of individual studies reflected in the results?	Yes
9. Were all the important outcomes considered?	Yes
10. Is any sponsorship/conflict of interest reported?	None
11. Finally…consider: Did the authors identify any limitations? Date of review – is it likely to be out of date? Are the conclusions the same in the abstract and the full text?	Ok

This checklist should be cited as:

Support Unit for Research Evidence (SURE) 2013. Questions to assist with the critical appraisal of a systematic review. Available at: http://www.cardiff.ac.uk/insrv/libraries/sure/doc/SURE_RCT_Checklist_2013.pdf

[1] Adapted and updated from the former Health Evidence Bulletins Wales (HEBW) checklist with reference to the NICE Public Health Methods Manual (2012) and previous versions of the Critical Appraisal Skills Programme (CASP) checklists.

Document cover sheet

Assessment report: MT241 UroLift Assessment Report Update

EAC team: Cedar (Laura Knight, Helen Morgan, Judith White, Megan Dale and Andrew Cleves)

Project lead(s): Dr Laura Knight

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EAC sign-off: Dr Rhys Morris

Version number	Brief description of changes	Author/reviewer (e.g. J Smith)	Date (DD/MM/YY)	Date sent to NICE (if applicable)
V0.1	Authoring	L Knight	27/07/2020	
V0.2	QA	J White	07/09/2020	
V0.3	Authoring – economics	M Dale and A Cleves	03/09/2020	
V0.4	Authoring and review	H Morgan	08/09/2020	
V0.5	Director sign-off	R Morris	09/09/2020	
V1.0	First draft to NICE	L Knight	09/09/2020	09/09/2020
V1.0 HU	NICE comments	Harriet Unsworth	10/09/2020	
V1.1	Addressing NICE comments	L Knight, M Dale and H Morgan	14/09/2020	
V1.2	Merging economic content	M Dale	15/09/2020	
V1.3	Director sign-off	R Morris	15/09/2020	15/09/2020
V1.4	Addressing company comments	L Knight and M Dale	21/09/2020	
V1.5	Director sign off	R Morris	22/09/2020	
V1.6	Additional edits by NICE	L Knight and M Dale	28/09/2020	

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technologies guidance
MT241 UroLift Assessment Report Update
External Assessment Centre report

Produced by: Cedar

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Date completed: V2.0 28/09/2020

Contains confidential information: Yes

Number of attached appendices: 5

Purpose of the assessment report

The purpose of this External Assessment Centre (EAC) report is to review and critically evaluate the company's clinical and economic evidence presented in the submission to support their case for adoption in the NHS. The report may also include additional analysis of the submitted evidence or new clinical and/or economic evidence. NICE has commissioned this work and provided the template for the report. The report forms part of the papers considered by the Medical Technologies Advisory Committee when it is making decisions about the guidance.

Declared interests of the authors

Description of any declared interests with related companies, and the matter under consideration. See NICE's Policy on managing interests for board members and employees.

If there are none, state 'none'.

Acknowledgements

Responsibility for report

The views expressed in this report are those of the authors and not those of NICE. Any errors are the responsibility of the authors.

Table of contents to be removed by NICE before including in the MTAC pack and publishing on the website.

Contents

Abbreviations

Term	Definition
ARU	Assessment report update
BPH	Benign prostatic hyperplasia
BPH-II	Benign prostatic hyperplasia Impact Index
EAC	External Assessment Centre
IIEF	International Index for Erectile Function
IPSS	International Prostate Symptom Score
IPSS-QoL	International Prostate Symptom Score – Quality of Life
ISI	Incontinence severity index
ITT	Intention to Treat
MHRA	Medicines & Healthcare products Regulatory Agency
MSHQ-EjD	Men's Sexual Health Questionnaire – Ejaculatory dysfunction
NHS	National Health Service
LUTS	Lower Urinary Tract Symptoms
NICE	National Institute for Health and Care Excellence
NICE CG	NICE clinical guideline
NICE MTG	NICE medical technology guidance
OML	Obstructive Medial Lobe
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PVP	photoselective vaporization of the prostate
PVR	Post-void residual
Qmax	Maximum urinary flow rate
QoL	Quality of Life
RCT	Randomised controlled trial
SHIM	Sexual health inventory for men
SLCS	Shared Learning Case Study
TURP	Transurethral resection of prostate

Executive summary

Clinical Evidence

New clinical evidence was submitted by the company for the purpose of this assessment report update (ARU). Following a review of the new evidence submitted and an updated search from the previous assessment report, 10 new studies, with 12 publications, were identified by the EAC and are included in this report. The evidence comprises 2 RCTs (each reported in 2 papers), 2 non-randomised comparative studies, 1 comparative crossover study and 5 non-comparative studies. In addition to this there are 3 NICE shared learning case studies (SLCS) included for reference.

One RCT was conducted in several countries in Europe, including the UK, and 1 was conducted in Northern America and Australia. Two of the comparative studies was conducted in the US with the other in Northern America and Australia. Of the non-comparative studies, one was conducted in the UK, 3 in Europe and one in Northern America and Australia. As only one of these was conducted solely in a UK/NHS setting and 1 partially, the results cannot be readily generalised to this setting.

Results were mixed and suggested that whilst UroLift improves symptoms over time, this improvement is not as big when compared to TURP for symptom severity and urological outcomes. However, UroLift appears to be superior compared to Rezum for symptom severity and erectile dysfunction and ejaculatory dysfunction measures. The quality of the included studies was moderate to high with most to all outcomes, participants and interventions being relevant to the scope. However, the majority of studies were conducted outside of the UK.

Economic evidence

The company submitted a de novo model based largely on evidence and parameters used in previous guidances (MTG26, MTG29, MTG49). The new model updated costs to more recent prices, the clinical parameters were updated to include five year outcomes for Urolift and median lobe treatment with Urolift was included. Rezum was also added as a comparator technology. There were a number of additional key changes in the model that are strong drivers of the outcome. These include a reduction in the number of Urolift devices used and reduction in theatre time required for Urolift. The evidence for these is based on [redacted] from NHS hospitals submitted by the company, but published evidence is more conservative.

Both the company and EAC base case are very slightly cost saving for UroLift compared to all other technologies. UroLift only remains cost saving compared to Rezum, where the key company assumptions are accepted, including a shorter

length of stay. UroLift remains cost saving in the model compared to the other technologies during one way sensitivity analysis and scenario modelling.

1 Decision problem

The company has not proposed any variation to the decision problem specified in the scope (see Table 1)

Table 1. Decision problem

Decision problem	Scope	EAC comment
Population	Men with lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) aged 45 or over, and with prostate volumes no greater than 100 ml	N/A
Intervention	The UroLift system in inpatient or day case setting	N/A
Comparator(s)	•Monopolar or bipolar transurethral resection of the prostate (TURP) •Holmium laser enucleation of the prostate (HoLEP) •Transurethral water vapour therapy using Rezum (NxThera Inc)	N/A
Outcomes	The outcome measures to consider include: •Length of hospital stay •The need for, or duration of, post-operative catheterisation •Number of post discharge follow-on consultations, both in primary and secondary care settings •Time to re-operation and re-operation rates •Symptoms of BPH (using the International Prostate Symptom Score [IPSS]) •Changes in ejaculatory or sexual function •Time to return to normal activities •Quality of life •Hospital-acquired infection •Theatre and staff time •Incidence of chronic atonic bladder, detrusor sphincter dyssynergia, chronic urinary infection, chronic renal failure •Device-related adverse events •Number of implants	N/A
Cost analysis	Comparator(s): Monopolar or bipolar TURP, HoLEP and Rezum Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be long enough to reflect differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers of implants and combinations of devices are needed.	N/A

Subgroups to be considered	Men for whom TURP or HoLEP is unsuitable because of operative risk including risks of blood loss or anaesthesia.	N/A
Special considerations, including those related to equality	Men who wish to preserve sexual function and fertility.	N/A
Special considerations, specifically related to equality	Are there any people with a protected characteristic for whom this device has a particularly disadvantageous impact or for whom this device will have a disproportionate impact on daily living, compared with people without that protected characteristic?	N/A
	Are there any changes that need to be considered in the scope to eliminate unlawful discrimination and to promote equality?	N/A
	Is there anything specific that needs to be done now to ensure the Medical Technologies Advisory Committee will have relevant information to consider equality issues when developing guidance?	N/A
Any other special considerations	Not applicable	N/A

2 Overview of the technology

The UroLift system (NeoTract) is used to perform a prostatic urethral lift, a procedure that is an alternative to current standard surgical interventions such as transurethral resection of the prostate (TURP) and holmium laser enucleation (HoLEP). The UroLift system uses adjustable, permanent implants to pull excess prostatic tissue away so that it does not narrow or block the urethra. In this way, the device is designed to relieve symptoms of urinary outflow obstruction without cutting or removing tissue.

The UroLift system comprises 2 single-use components: a delivery device and an implant. The delivery device consists of a hand-held pistol grip to which a needle-shaped probe is attached. Each UroLift implant consists of a superelastic nitinol capsular tab, a polyethylene terephthalate monofilament, and a stainless steel urethral end-piece. The surgeon inserts the probe into the urethra until it reaches the prostatic urethra (the widest part of the urethral canal); a fine needle at the end of the probe deploys and secures an implant in a lobe of the prostate. One end of the implant is anchored in the urethra and the other is attached to the firm outer surface of the prostatic capsule, so pulling the prostatic lobe away from the urethra. This is repeated on the other lobe of the prostate. Typically about 3.5 implants are used. The procedure can be done with the patient under local or general anaesthetic and may be done either as an in-patient or day-case basis.

The company has confirmed that there have been no changes to the technology and the CE mark is up to date.

3 Clinical context

Urolift is intended for use for the treatment of symptoms due to urinary outflow obstruction or lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH), including lateral and median lobe hyperplasia, in men 50 years of age or older. It is contraindicated for those who have a prostate volume of more than 100 ml, or those who have a urinary tract infection, urethral conditions that prevent the insertion of the delivery system into the bladder, urinary incontinence due to incompetent sphincter, or current gross haematuria. The company states that UroLift is increasingly performed under local anaesthetic, without an anaesthetist present, with light sedation if needed.

Current treatment options for benign prostatic hyperplasia when conservative management options have been unsuccessful or are not appropriate in the NICE guideline on lower urinary tract symptoms (CG97) include:

- Monopolar or bipolar transurethral resection of the prostate (TURP)
- Transurethral vapourisation of the prostate (TUVP)
- Holmium laser enucleation of the prostate (HoLEP; at centres specialising in the technique or with mentorship arrangements in place)
- Transurethral incision of the prostate (TUIP; only in prostates smaller than 30 ml)
- Open prostatectomy (only in prostates larger than 80 ml).

Rezum, which is a water vapour (steam) therapy for treating LUTS secondary to BPH, destroys excess prostate tissue with the aim of relieving symptoms. Rezum for treating lower urinary tract symptoms secondary to benign prostatic hyperplasia (NICE MTG 49) suggests this procedure can also be used for people with moderate to severe LUTS, as shown by an International Prostate Symptoms Score (IPSS) of 13 or over and, a moderately enlarged prostate (typically between 30 cm^3 and 80 cm^3).

UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia (NICE MTG26) states the UroLift system should be considered as an alternative to current surgical procedures for use in a day-case setting in men with lower urinary tract symptoms of benign prostatic hyperplasia who are aged 50 years and older and who have a prostate of less than 100 ml without an obstructing middle lobe.

If offering surgery for managing voiding LUTS presumed secondary to BPH, only consider offering laser vaporisation techniques, bipolar TUVP or monopolar or bipolar transurethral vaporisation resection of the prostate (TUVRP) as part of a randomised controlled trial that compares these techniques with TURP. Surgery for managing voiding LUTS presumed secondary to BPH, should only be consider offering botulinum toxin injection into the prostate as part of a randomised controlled trial. The clinical guideline also recommends offering adjustable prostatic implants (such as the UroLift system) for the treatment of storage symptoms only as part of a randomised controlled trial. Insertion of prostatic urethral lift implants to treat lower urinary tract symptoms secondary to benign prostatic hyperplasia (NICE IPG 475) concluded that there is adequate evidence on the safety and efficacy of the procedure to support its use, provided that clinicians have specific training in the insertion of the implants.

Minimally invasive treatments such as transurethral needle ablation (TUNA), transurethral microwave thermotherapy (TUMT), high-intensity focused ultrasound (HIFU), transurethral ethanol ablation of the prostate (TEAP) and laser coagulation are not recommended by NICE for people with LUTS.

Special considerations, including issues related to equality

The company identified three areas related to equality for consideration:

- Age: The prevalence of LUTS secondary to BPH increases with advancing age. Elderly men are the most common group of patients requiring surgical treatment for LUTS/BPH. Advanced age is an independent predictor of adverse outcomes after all surgery, including for BPH. However, as this procedure is classed as low risk, UroLift is associated with a lower risk of complications compared to standard resection procedures.

- Gender: Teleflex is aware of 8 patients (worldwide, one NHS) who identify as female who have undergone the UroLift procedure.

- Race: People of non-white family origin has been shown to be an independent predictor of adverse outcomes following BPH surgery. However, as this procedure is classed as low risk, UroLift is associated with a lower risk of complications compared to standard resection procedures.

The EAC did not identify any further areas for consideration.

4 Clinical evidence selection

4.1 *Evidence search strategy and study selection*

The company did not update their search strategy for the purpose of this assessment report (AR) update, however NICE conducted searches for an interim review of the guidance. The interim review searches were based on the searches conducted for the original assessment report and were completed on 31st July 2019. Please see Ray et al (2015) for critique of the original company search strategies.

To ensure that the EAC had access to all literature since the original assessment report was conducted, an update search for this ARU was conducted, using the search strategy for the original assessment report. These searches were conducted on 14th July 2020 in the following databases: Medline ALL (Ovid), EMBASE (Ovid), Cochrane Database of Systematic Reviews, CENTRAL, HTA and NHS EED (CRD). Searches were also conducted for ongoing trials in Clinical Trials.gov, WHO International Clinical Trials Registry Platform and of the Company's website. In addition, the MHRA's resource for medical device alerts and field safety notices and the MAUDE database were searched for adverse events. The EAC update

search identified 427 references, 129 adverse event reports and 2 ongoing trials. A pragmatic decision was taken to only screen evidence that had been published since NICE's interim review in July 2019.

4.2 *Included and excluded studies*

The studies submitted to the EAC by the company are listed in Table 2 together with the EAC's selection decision. The EAC identified 12 publications (from 10 studies) for full-text review, 11 of which were not selected by the company, but were deemed relevant to the scope of this guidance update and have been included in Table 3.

Table 2: Studies submitted by the company

	Study	**EAC Decision**
Published	Rochester et al (2019)	**Exclude** – indication of acute urinary retention (AUR) outside of scope
	NICE shared learning case studies	**Include –** see Table 6
	Young et al - **Abstract**	**Exclude** – lack of reported clinical outcomes outside of scope
	Tutrone and Schiff (2020)	**Include –** See Table 5
Unpublished	[redacted] **Abstract**	**Exclude –** As this is unpublished, there are no details available for extraction
	[redacted] **Abstract**	**Exclude** – indication of acute urinary retention (AUR) outside of scope
	[redacted] **Abstract**	**Exclude** – indication of acute urinary retention (AUR) outside of scope
	[redacted] **Abstract**	**Exclude –** As this is unpublished, there are no details available for extraction

Table 3: Studies selected by the EAC as the evidence base

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAC comments

Roehrborm et al (2015) L.I.F.T study – three year follow-up USA Canada Australia	The Luminal Improvement Following Prostatic Tissue Approximation for the Treatment of LUTs secondary to BPH (L.I.F.T study) was a prospective, randomised, controlled, blinded study **Intervention**: Active PUL (UroLift) **Control**: Sham procedure **Inclusion criteria:** • Male gender • Diagnosis of symptomatic BPH • Age ≥ 50 years • IPSS ≥ 13 • Peak urine flow rate ≤ 12mL/sec on a voided volume ≥ 125 mL • Prostate volume ≥ 30 cc to ≤80 cc per ultrasound • Prostate length measurement of ≥ 30mm and ≤80 mm **Exclusion criteria:** • Current urinary retention • Post void residual (PVR) urine >250ml	206 male participants were randomised 2:1 to receive either Active PUL (UroLift) or the control sham procedure **Active PUL (Urolift) n** = 140, mean age 67 years (93 included for effective analysis at 3 years) **Control sham procedure n** = 66, mean age 64 years **Three-year follow-up only in PUL group compared to baseline**	Three-year follow-up: • IPSS score • IPSS QoL score • BPHII: BPH Impact Index • Peak flow rate (Qmax) • Sexual function (SHIM: Sexual Health Inventory for Men and MSHQ-EjD: Male Sexual Health Questionnaire for Ejaculatory Dysfunction) • Adverse events	Randomisation procedure used permuted blocks of various sizes chosen at random through a password protected electronic database Study was powered for the primary endpoint assuming a t-test comparison of mean values with 0.05 two-sided type 1 error and 80% statistical power

	• Obstructive or protruding median lobe of the prostate • Active urinary tract infection (UTI) at the time of treatment • Previous BPH procedure • Urethral conditions that may prevent insertion and delivery of device system into bladder (i.e. strictures, meatal stenosis, bladder neck contracture) • Urinary incontinence • Biopsy of the prostate within the last 6 weeks **Funding:** Not reported **Status:** Published			

Sonksen (2015) The BPH6 study. Denmark UK Germany Italy Feb 2012 – Oct 2013	Multicentre, prospective, randomised controlled trial at 10 European centres **Intervention**: Prostatic Urethral Lift (PUL) using UroLift **Comparator**: Transurethral resection of the prostate (TURP) **Inclusion criteria:** •Male aged ≥50 yr •International Prostate Symptom Score >12 •Qmax ≤15 ml/s for 125-ml voided volume •Post-void residual volume <350 ml •Prostate volume ≤60 cm^3 on ultrasound •Sexually active within 6 months before the index procedure **Exclusion criteria** •Active urinary tract infection at time of treatment	80 men with LUTS secondary to BPH were randomised 1:1 to either PUL (UroLift) or TURP **PUL (UroLift) n** = 45 (46 randomised, 1 declined treatment), 44 included in analysis due to 1 protocol deviation, mean age 63 years. **TURP n** = 35 (45 randomised, 10 declined treatment), mean age 65 years	Primary study endpoint was a composite of 6 elements that assess overall outcome One-year follow-up: • IPSS score • Quality of Recovery visual analogue score (QoR VAS) • Sexual Health Inventory for Men (SHIM) • MSHQ-EjD • Incontinence Severity Index (ISI) • Adverse events Secondary endpoints: •IPSS score •IPSS QoL score •BPH II •Qmax •PVR	The study was powered to establish noninferiority of PUL to TURP for noninferiority delta of 10% for the BPH6 primary endpoint. Performance estimates from the literature predicted that power of 80% would be achieved with enrolment of 62 participants, assuming the BPH6 success rate was 51% and 30% for PUL and TURP, respectively. Parallel randomization was conducted at a ratio of 1:1 at the time of the procedure, stratified by site, and performed using permuted blocks of various sizes chosen at random and concealed through a password-protected computer database Funded by manufacturer

	• Bacterial prostatitis within 1 year of the index procedure • Cystolithiasis within 3 months of the index procedure • Obstructive median lobe, as assessed via ultrasound and cystoscopy • Current urinary retention **Funding:** NeoTract Inc. **Status**: Published			

Bozkurt (2016) Turkey Mar 2011-Jun 2015	Retrospective non-comparative study **Intervention**: UroLift **Inclusion criteria:** • Diagnosis of BPH and had undergone the UroLift procedure **Exclusion criteria:** •Prostate median lobe in TRUS •LUTS due to reasons other than BPH •Neurogenic bladder •PSA >4 ng/dl •Previous prostatic surgery •Active urinary system infection •History of bladder diseases, •Prostate volume >100 g •IPPS <12, PVR >350 ml •Qmax>15 ml/s in UFM **Funding**: Not reported	17 patients diagnosed with BPH (mean age 67 years) who had undergone the UroLift procedure were retrospectively evaluated.	**Up to one-year follow-up:** •IPSS •Uroflowmetry •QoL index •International Index of Erectile Function (IIEF) •MSHQ-EjD	Low sample size

	Status: Published			
Gratzke et al (2016) **The BPH6 study.** Germany UK Denmark Feb 2012-Oct 2013	Prospective, randomised, controlled, non-blinded study at 10 European centres in 3 countries **Intervention**: PUL (UroLift) **Control**: TURP **Inclusion criteria:** • Age ≥ 50 years and a candidate for TURP • IPSS >12 • Qmax ≤15 mL/s • Prostate volume ≤ 60 cc on ultrasonography **Exclusion criteria**: Not reported **Funding**: Not reported **Status**: Published	80 patients were randomised 1:1 to either PUL (UroLift) or TURP. Number of patients randomised to each group not reported. Number of patients contributing data to each outcome reported. From Sønsksen et al. (2015) 45 in PUL arm and 35 in TURP arm (BPH6 study). **PUL (UroLift) n** = 45, mean age 63 years **TURP n** = 35, mean age 65 years	**Two-year BPH6 follow-up:** • IPSS score • Sexual Health Inventory for Men (SHIM) • MSHQ-WjD • Incontinence Severity Index (ISI) • Adverse events **Secondary outcomes:** • PGI-I questionnaire • SF-12 • SF-6D	Sample size and n's reported for each group do not match

Rukstalis et al (2016) L.I.F.T study follow-up (see Roehrborn et al (2015)	Open-label, crossover study looking at 24-month durability after crossover to PUL following blinded control sham procedure in the L.I.F.T study. After 3 month follow-up, patients were unblinded and offered enrolment in crossover study during which they received PUL treatment and were followed by 24 months. **Procedure 1** = Sham **Crossover procedure =** PUL (UroLift) **Inclusion criteria:** • Aged >50 years, • IPSS of ≥13 • Qmax ≤12 mL/s on a voided volume of 125 Ml • Prostate volume of 30–80 mL • Provided informed consent **Exclusion criteria:** • Prior surgical BPH treatment • Obstructive median lobe	51 patients who had previously undergone a sham procedure as part of the L.I.F.T study (mean age 64 years)	**3-month post sham outcomes**: • IPSS • Qmax • IPSS QoL • BPH II • PVR • SHIM questionnaire **24 month outcomes after cross-over to PUL**	Funded by manufacturer

	• Current urinary retention • PVR ≥250 mL • Active UTI • PSA level of >10 ng/mL unless negative biopsy for cancer • Cystolithiasis within 3 months • Bacterial prostatitis within 1 year • History of prostate or bladder cancer **Funding**: NeoTract Inc **Status**: Published			

Bardoli et al (2017) UK April 2016 – no end date reported	Single centre, single surgeon retrospective note analysis **Intervention**: UroLift **Inclusion criteria:** • Age >50 years • IPSS ≥10 • Qmax ≤ 14ml/s • Prostate volume and middle lobe assessed by flexible cystoscopy and digital rectal exam **Exclusion criteria:** • In retention with a catheter • Large median lobe on flexible cystoscopy • Prostatic volume > 80cc • Suspected neurological conditions that could affect voiding **Funding**: Not reported **Status**: Published	11 patients from 52 identified who were eligible for TURP were deemed suitable for the UroLift procedure (mean age 70.5 years)	**Baseline and 4 month post-operative data:** • IPSS • Quality of life • PVR • Qmax	

Roehrborn et al (2017) L.I.F.T study – 5-year follow-up	5 year follow-up from L.I.F.T study. Prospective, randomised, controlled, blinded study. See Roehrborn et al (2015)	87/140 patients were available for per protocol analysis from the PUL group at 5 years. 96 patients available at 49-60 months. Mean age not reported. Missing data at 5 years was imputed using last observation carried forward. Only results from those still remaining in the PUL group were analysed at 5-years	60 month follow-up: • IPSS • IPSS-QoL • Qmax • BPHII • MSHQ-EjD • IIEF-5	Reporting of sample size is inconsistent throughout
Rukstalis et al (2018) MedLift study USA	12 month follow-up from MedLift study. Is a cohort extension of the L.I.F.T study looking at only those with obstructive middle lobes (OML) See Roehrborn et al (2015) Intervention = UroLift in obstructive medial lobe (OML) patients Additional comparative analysis:r = UroLift in both OML and lateral lobe (LL) patients Funding: NeoTract/Teleflex Inc.	Intervnetion n = 45 patients enrolled from 71 identified. Results were also presented, and compared for a group that included both LL patients from the L.I.F.T. study and the OML patients from the intervention arm n=181 for IPSS at 3 months.	12-month follow-up: • IPSS • QoL • BPH-II • Qmax • IIEF • MSHQ-EjD • SHIM • Adverse events	The study was powered to have 95% probability of establishing the true percent improvement in IPSS score from baseline to 6 months was greater than 25%, with 95% confidence. The minimum required number of evaluable subjects was determined to be 35. Funded by manufacturer

Eure et al (2019) USA Australia July 2017 – Sept 2018	Retrospective multicentre chart analysis across 14 centres. **Intervention**: PUL (UroLift) **Inclusion criteria:** • Documented baseline IPSS score ≤ 9 months before PUL • At least one post-procedure IPSS within 12 months of treatment. **Exclusion criteria**: Not reported **Funding**: NeoTract Inc **Status**: Published	1413 consecutive patients who received PUL as part of a real-world retrospective (RWR) study split into Group A (nonurinary retention) and Group B (urinary retention). These were compared with the PUL group from the L.I.F.T study at 5-year follow-up **RWR n** = 1413 (mean age 70 years) • Group A n = 1248 • Group B n = 165 **L.I.F.T n** = 140 (mean age 67 years)	Follow-up at 1, 3, 6, 12 and 24 months post-operatively. • IPSS • IPSS QoL • Qmax • PVR • PSA • Prostate volume • Implants per subject	Given 5-year n from L.I.F.T study does not match the n reported in Roerhborn et al (2017) There is minimal reported outcomes comparing Group A and B Funded by manufacturer

Sievert et al (2019) Germany Oct 2010 – June 2014	Multicentre prospective non-comparative study across 5 sites **Intervention** = PUL (UroLift) **Inclusion criteria** • Patients with confirmed moderate-to-severe Benign Prostatic Obstruction (BPO) that were unresponsive to oral therapy • Eligible for surgical ablation using TURP **Exclusion criteria:** • Obstructive median lobe seen during cystoscopy **Funding**: No funding provided **Status**: Published	138 patients were eligible and of these 86 chose to have the PUL procedure (mean age 66.2 years)	Follow-up at 1, 6, 12 and 24 months post-operatively. • IPSS • IPSS QoL • PVR • Qmax • Adverse events	

Rubio et al (2019) Spain April 2017 and April 2018	Non-comparative prospective study across 2 centres **Intervention** = UroLift **Inclusion criteria:** • Prostate volume <60 cc • Moderate symptoms of BPH with an IPSS >12 • Qmax <15ml/s **Exclusion criteria:** • Middle lobe or high bladder neck in urethrocystoscopy • Positive urine culture **Funding**: Not reported **Status**: Published 	20 patients treated with UroLift (mean age 61.2 years) 	Follow-up at 1 month and 3 months. • Tolerability of the procedure as a day case under local anaesthetic • IPSS • Qmax • IIEF • Adverse events 	Low sample size

Tutrone and Schiff (2020) USA No dates reported	Non-randomised, prospective, comparative study across two study sites **Intervention**: UroLift **Comparator**: Rezum **Inclusion criteria:** • Undergone either UroLift or Rezum procedure within the last 2 months. • Urolift indicated for men aged ≥ 45 and prostates ≤ 100 cc ith no lower limit. • Rezum indicated for men ages ≥ 50 and prostates ≥ 30 cc and ≤ 80 cc. **Exclusion criteria:** • None **Funding:** Sponsored by NeoTract/Teleflex **Status**: Published	53 male patients: **UroLift**: n=30 (mean age 68 years; prostate volume 49cc) **Rezum** n = 23 (mean age 69 years; prostate volume 63cc)	Questionnaires completed an average of 30 days post procedure • IPSS • IPSS QoL • SHIM • MSHQ-EjD • MSHQ-EjD (bother)	Relatively low sample sizes Sponsored by the manufacturer

IIEF: International Index for Erectile Function; IPSS: International Prostate Symptom Score; IPSS QoL: International Prostate Symptom Score – Quality of Life; MSHQ-EjD: Men's Sexual Health Questionnaire – Ejaculatory Dysfunction; PVR: Post-void Residual; Qmax: Maximum urinary flow rate; SHIM: Sexual Health Inventory for Men;

5 Clinical evidence review

5.1 *Overview of methodologies of all included studies*

There are 11 publications of 9 studies included in this ARU of which 6 were comparative; 4 were RCT's from 2 studies(Roehrborn et al ; 2015 and 2017, Sonksen et al; 2015 and Gratzke; 2016), 2 were prospective comparative studies (Rukstalis et al; 2018 and Tutrone and Schiff; 2020), 1 was a crossover study (Rukstalis et al; 2016) and 5 were non-comparative in design (Bozkurt et al; 2016, Bardoli et al; 2017, Eure et al; 2019, Sievert et al; 2019 and Rubio et al; 2019).

5.2 *Critical appraisal of studies and review of company's critical appraisal*

Most of the included studies were moderate or high quality with direct comparisons, correct patient population and/or blinded procedures. The 2 publications reporting results from the L.I.F.T study (Roehrborn et al; 2015 ad 2017) were deemed to have a low risk of bias with both patients and assessors blinded to procedure and outcome. However, there were some concerns of bias with the 2 publications from the BPH6 study (Sonksen et al; 2015 and Gratzke et al 2016) as the study was not blinded to patient or assessor and ITT analysis was not specified which, if not done, could have impacted the results.

The non-randomised crossover and comparative studies (Rukstalis et al; 2016, Rukstalis et al; 2018 and Tutrone and Schiff; 2020) were also deemed low risk apart from the fact that they were non-randomised. As the Rukstalis study is a crossover study some of the appraisal questions were not directly relevant (i.e. in relation to control groups and treatment of groups) but no major concerns were identified.

The main issues were from the non-comparative studies with several (Bozkurt et al; 2016, Bardoli et al; 2017 and Rubio et al; 2019) having very low ($\leq$20) sample sizes, some reporting very limited or no inclusion/exclusion criteria (Eure et al; 2019 and Sievert et al; 2019), one not reporting outcome measures clearly in the methods (Bardoli et al; 2017) and none reporting whether the study was blinded in anyway. However, two studies were deemed to be of good quality overall (Bozkurt et al; 2016 and Rubio et al 2019).

5.3 *Results from the evidence base*

Table 5 summarises the results from the included studies. As there are many different measures with improvements not always in the same direction, Table 4 shows which direction of scoring equals improvement.

Table 4: Included measures and direction of improvement

Measure	Symptom	Direction of improvement in scores
BPH-II	BPH Symptom severity	Decrease
ISI	Incontinence	Decrease
MSHQ-EjD function	Sexual health and ejaculatory function	Increase
IIEF and SHIM	Erectile dysfunction	Increase
IPSS	Prostate symptom severity	Decrease
Qmax	Maximum urinary flow	Increase
PVR	Post urination residual volume	Decrease
QoL	Quality of life	Decrease

Table 5: Results of included studies

Study	BPH Impact Index (BPH II)	Incontinence (ISI)	Erectile and sexual dysfunction (MSHQ, MSHQ-EjD, IIEF and SHIM)	IPSS	Maximum urinary flow rate (Q_{max} (mL/s)) and postvoid residual volume (PVR (mL))	IPSS-Quality of life (QoL)	Operation time (mean minutes), number of implants and Time to discharge (mean days)	Catheterisation rate and length (mean days)
Roehrborn et al (2015) **L.I.F.T 3-year follow-up**	Percentage change from baseline to 3-years was decreased 53.2%, p<0.0001	Not reported	No significant differences in change in SHIM score from baseline and 3 year follow-up MSHQ-EjD function change was 8.9% from baseline (p=0.0129) and MSHQ-EjD Bother change was -27.4% from baseline (p=0.0002) to 3 years.	Percentage decrease from baseline to 3-years of 41.1%, p<0.0001	Qmax percentage increase from baseline to 3-years of 53.1%, p<0.0001 PVR percentage change not significantly different.	Percentage change from baseline to 3-years decreased 48.8%, p<0.0001	Operation time was 66.16 minutes for UroLift compared to 46.86 minutes for the sham procedure. Mean number of implants was 5.2 Time to discharge was 0.19 days for UroLift and 0.16 days for the sham procedure.	32% of UroLift patients required catheterisation with an average 0.9 catheterisation days reported for the cohort as a whole

Sonksen et al (2015)	No significant differences between UroLift and TURP at any of the follow-up time points	In the TURP group, patients experienced a significant worsening at both 2 weeks and 3 months. No values given. Continence preservation was comparable between the groups, and no patient experienced new-onset stress or sphincter incontinence. Of the participants who failed the BPH6 continence element (six PUL and eight TURP patients had ISI > 4 at any time), none	No significant differences in change in SHIM score from baseline UroLift and TURP at any of the follow-up time points. Significant differences in MSHQ-EjD function at 1 month (UroLift change from 10.6 to 12.3 and TURP 8.6 to 7.7, p = 0.03), 3 months (UroLift 10.8 to 11.5 and TURP 9.3 to 6.3, p = 0.0002), 6 months (UroLift 10.8 to 11.9 and TURP 8.9 to 5.7, p	No significant differences between UroLift and TURP at 2 weeks, 1, 3 and 6 months. At 12 month follow-up, UroLift score (10.7) was significantly higher than TURP (7.3), p=0.02	Significant differences in change from baseline in Qmax at 3 months (UroLift change from 9.4 to 13.6 and TURP 9.2 to 22.6, p <0.0001), 6 months (UroLift 9.6 to 13.5 and TURP 9.4 to 19.0, p=0.003) and 12 months (UroLift 9.6 to 13.6 and TURP 9.5 to 23.2, p <0.0001). Significant differences in change from baseline in PVR at 3 months	No significant differences between UroLift and TURP at any of the follow-up time-points	Time to discharge was 1.0 days for UroLift compared to 1.9 days for TURP Mean number of implants was 4.7 Anaesthesia time was 55 minutes for UroLift and 71 minutes for TURP	74% of the TURP group required catheterisation for >24 hours compared to 45% of the UroLift group (p=0.01)

		of the PUL patients reported new-onset pad use, whereas 6 TURP patients (6/8, 75%) reported that they required pads after TURP (superior PUL performance, p = 0.01).	<0.0001) and 12 months (UroLift 10.6 to 11.9 and TURP 9.3 to 5.6, p <0.0001). No significant differences for MSHQ-EjD bother at 1, 6 and 12 months. Significant differences at 3 months (UroLift 1.7 to 1.1 and TURP 1.9 to 2.1, p = 0.01).		(UroLift change from 87.6 to 77.3 and TURP 98.6 to 47.6, p=0.002), 6 months (UroLift 85.5 to 80.7 and TURP 100.5 to 46.2, p = 0.003) and 12 months (UroLift 86.3 to 93.7 and TURP 103.5 to 33.6, p = 0.002).			
Bozkurt et al (2016)	Not reported	Not reported	IIEF scores were not significantly different between baseline, 3 and 12 months MSHQ-EjD scores were not	Significant differences in IPSS scores between baseline (22.8), 3 months (13.3, p <0.001) and 12 months (13.2, p <0.001). No significant	Significant differences were found for Qmax between baseline (7.6), 3 months (11.5, p<0.001) and 12 months (11.8, p<0.001). No	QoL scores significantly improved from baseline (3.17) to 3 months (2.23, p=0.001) and 12 months (2.29, p = 0.001).	Operation time was 29.1 minutes. Mean number of implants was 3.71 All patients were discharged within 1 day.	No patients required catheterisation post procedure

			significantly different between baseline, 3 and 12 months	difference was found between 3 and 12 months	significant difference between 3 and 12 months Significant differences were found for PVR between baseline (50.3), 3 months (35.4, p<0.001) and 12 months (35.8, p<0.001). No significant differences between 3 and 12 months			
Gratzke et al (2016)	No significant differences between groups at any follow-up.	Average ISI score was consistent throughout follow-up for the UroLift group and did not change significantly from baseline at any time point. No figures or p-values were	No significant differences in the change from baseline in SHIM scores between groups at any follow-up. No significant difference in the change	No significant differences in the change from baseline in IPSS scores between groups at 2 weeks, 1, 3 and 6 months. Significant differences in the change in	Significant differences between groups in the change in baseline for Qmax at 3 months (UroLift 9.4 to 13.6 and TURP 9.0 to 21.7, p<0.001), 6	No significant differences from baseline between groups at any follow-up.		

		given.	from baseline in MSHQ-EjD bother scores between groups at any follow-up. Significant differences in change in MHSQ-EjD function from baseline to 1 month (UroLift 10.6 to 12.3 and TURP 8.6 to 7.7, p=0.049), 3 months (UroLift 10.8 to11.5 and TURP 9.3 to 6.3, p <0.001), 6 months (UroLift 10.8 to 11.9 and TURP 8.9 to 5.7, p <0.001), 12 months (UroLift 10.6 to 11.9 and TURP 9.3 to 5.6, p <0.001) and 24 months (UroLift 10.6to	IPSS scores from baseline between groups at 12 months (UroLift 21.8 to 10.9 and TURP 22.8 to 7.3, p=0.013) and 24 months (UroLift 21.4 to 12.2 and TURP 22.8 to 7.4, p = 0.004).	months (UroLift 9.6 to 13.5 and TURP 9.4 to 19.0, p=0.003), 12 months (UroLift 9.6 to 13.6 and TURP 9.5 to 23.2, p<0.001) and 24 months (UroLift 9.3 to 14.3 and TURP 9.6 to 25.5, p=0.002). Significant differences in the change from baseline in PVR at 3 months (UroLift 87.6 to 77.3 and TURP 98.6 to 47.6, p = 0.014), 6 months (UroLift 85.5 to 80.7 and TURP 100.5 to 46.2, p = 0.009) and 12			

			10.9 and TURP 8.9 to 4.9, p <0.001).		months (UroLift 86.3 to 93.7 and TURP 103.5 to 33.6, p <0.002). No significant difference was seen at 24 months.			
Rukstalis et al (2016)	Significant differences in BPHII from baseline to 1 month (change from 7.33 to 3.24), 3 months (7.32 to 2.94), 6 months (7.33 to 2.84), 12 months (7.43 to 3.43) and 24 months (7.12 to 3.19), all p <0.001. No significant difference at 0.5 months.		No significant differences were found for SHIM scores from baseline to any follow-up. Significant differences for MSHQ-EjD function from baseline to 1 month (change from 8.71 to 11.56) 3 months (8.86 to 11.19), 6 months (8.82 to 11.11), 12 months (8.88 to 10.94) and	Significant differences in IPSS scores from baseline to 0.5 months (change from 25.41 to 18.92), 1 month (25.41 to12.43), 3 months (25.44 to 12.32), 6 months (25.41 to 13.06), 12 months (25.49 to 15.22) and 24 months (24.76 to 15.17), all p <0.001.	Significant differences in Qmax from baseline to 3 months (7.95 to 11.95), 12 months (8.09 to12.07) and 24 months (8.00 to 12.18), all p <0.001 Significant differences in PVR from baseline to 3 months (change from 89.26 to 52.95, p=0.003) and 12 months	Significant differences in QoL from baseline to 0.5 months (change from 4.80 to 3.43) 1 month (4.80 to 2.35), 3 months (4.78 to 2.18), 6 months (4.80 to 2.45), 12 months (4.78 to 2.73) and 24 months (4.64 to 2.64), all p <0.001.	Anaesthesia time was 51.25 minutes Mean number of implants was 4.5 Time to discharge was 0.21 days	

			12 months (8.94 to 10.65), all p <0.001.		(87.98 to 56.74, p=0.004). No significant difference found at 24 months compared to baseline (86.55 to 79.23).			
Bardoli et al (2017)				Significant decrease in IPSS score from baseline (25.4) to 4 months (16.3, p=0.02).	Significant decrease in PVR from baseline (300.1) to 4 months (193.8, p=0.04). No significant difference for Qmax.	Significant decrease in QoL from baseline (5.1) to 4 months (3.5, p=0.04).	Operation time was 8.5 minutes Mean number of implants was 4.0 Hospitalisation time was 0.44 days	
Roehrborn et al (2017) **L.I.F.T 5-year follow-up**	Significant decrease in BPHII from baseline (6.92) to 5-year follow-up (3.51,			Significant decrease in IPSS from baseline (22.32) to 5-year follow-up (14.47,	Significant increase in Qmax from baseline (7.88) to 5-year follow-up (11.08, p<0.0001)	Significant decrease in QoL from baseline (4.62) to 5-year follow-up (2.54,		

	p<0.0001)			p<0.0001)		p<0.0001)		
Rukstalis et al (2018)	In the OML only group, there was a significant decrease from baseline (7.7) and 1 month (3.7), 3 months (1.8), 6 months (1.7) and 12 months (2.1), all p<0.0001 In the Combined group there was a significant decrease from baseline (7-7.1) and 1 month (3.9), 3 months (2.6), 6 months (2.4) and 12 months (2.6), all p<0.0001 The size of the % change was significantly		For MSHQ-EjD function, in the OML group there was a significant increase from baseline (9.2-9.4) and 1 month (11.4), 3 months (11.3), 6 months (11.2) and 12 months (11.4), all p<0.0026 In the combined group there was a significant increase from baseline (8.9-9) and 1 month (11.3), 3 months (11.1), 6 months (10.7) and 12 months (10.6),	In the OML group, IPSS scores showed a significant decrease from baseline (24.1-24.2) and 1 month (9.8), 3 months (8.3), 6 months (10.0) and 12 months (10.6), all p<0.0001 In the combined group there was a significant decrease from baseline (22.7-22.8) and 1 month (11.7), 3 months (10.4), 6 months (10.9) and 12 months (11.3), all p<0.00001	In the OML group Qmax scores significantly increased from baseline (7.1-7.2) compared to 1 month (15) 3 months (14.6), 6 months (12.3) and 12 months (13.5), all p<0.0001 In the combined group there was a significant increase from baseline (7.1-7.8) and 1 month (15), 3 months (12.9), 6 months (12.3) and 12 months (12.5), all p<0.00001	In the OML group QoL scores significantly decreased from baseline (4.9) compared to 1 month (1.8), 3 months (1.6), 6 months (1.9) and 12 months (1.9), all p<0.0001 In the combined group there was a significant decrease from baseline (4.7)) and 1 month (2.4), 3 months (2.2), 6 months (2.1) and 12 months (2.2), all p<0.00001 The % change was	Operation time not reported Mean length of stay was 2.4 hours Mean number of implants was 6.3	29/45 (64.4%) were catheterised post-operatively. A further 7 (15.6%) required catheterisation prior to discharge. Mean duration of catheterisation was 1.2 days

	bigger in the OML group compared to the combined group at each time point (p=0.05-0.0007)		all p<0.00001 The size of the %change did not differ between groups at any time point For MSHQ-EjD bother, in the OML group there was a significant decrease from baseline (1.6) and 1 month (1.1), 3 months (0.7), 6 months (0.6) and 12 months (0.9), p-values 0.02-<0.0001 In the combined group there was a significant decrease from baseline (2.0)	The % change was significantly bigger in the OML group compared to the combined group at every time point, especially 1 and 3 months (p=0.03-0.0003)	Differences in % change was only reported for 3 and 12 months where it was significantly bigger in the OML group at 3 months only (p=0.002) At 1 month and 6 months the number of patients is the same in both the OML and combined group (n=37 and n=41 respectively).	significantly bigger in the OML group compared to the combined group at every time point, (p=0.01-0.0003) except at 6 months where no difference was found.		

			and 1 month (1.2), 3 months (1.0), 6 months (1.1) and 12 months (1.3), all p<0.00001 The size of the %change did not differ between groups at any time point For the IIEF, in the OML group there was no significant difference in scores from baseline (21.8 - 22.5) to any time-point. In the combined group there was a significant increase from baseline (20.5					

			- 21.0) and 1 month (22.0) and 3 months (22.2), p=0.02 and 0.004 respectively. There was no significant differences at 6 months and 12 months. The size of the %change did not differ between groups at any time point For the SHIM results, In the OML group there was a significant increase from baseline (17.2-17.6) and 3 months (18.7) and 12 months (18.4), p=0.05 and 0.04 respectively.					

			No significant differences were found between baseline and 1 and 6 months. In the combined group there was a significant increase from baseline (16.4-16.7) and 1 month (17.6), 3 months (17.8), and 12 months (17.2), p=0.002-0.05. There was no significant difference at 1 month. The size of the %change did not differ between groups at any time point					

Sievert et al (2018)				Significant decreases in IPSS from baseline (20.82) to 1 month (11.92), 6 months (10.59), 12 months (10.29) and 24 months follow-up (10.17), all p<0.0001.	Significant decreases in PVR from baseline (149.53) to 6 months (50.85, p<0.01), 12 months (62.97, p<0.005) and 24 months follow-up (44.63, p<0.01). No significant difference found at 1-month. Significant increases for Qmax from baseline (11.24) to 1 month (15.54, p=0.005), 6 months (14.95, p<0.001), 12 months (14.11, p<0.001) and 24 months follow-up	Significant decreases in QoL from baseline (4.14) to 1 month (2.22), 6 months (2.05), 12 months (2.21) and 24 months follow-up (1.98), all p<0.0001.	Mean operation time was 57 minutes Mean number of implants was 3.8 Mean hospitalisation time was 2.0 days	

					(14.21, p=0.005).			
Eure et al (2019)				Significant decrease in IPSS scores between baseline and 1 month (change from 19.3 to 10.7), 3 months (19.1 to 10.4), 6 months (219.1 to 10.4), 12 months (19.1 to 11.0) and 24 months (19.5 to 11.2), all p<0.0001.	Significant decrease in Qmax between baseline and 1 month (change from 13.2 to 11.9, p=0.02), 3 months (13.1 to 10.8, p<0.01) and 6 months (13.4 to 11.1, p=0.03). No significant differences at 12 and 24 months follow-up.	Significant decrease in QoL between baseline and 1 month (change from 4.0 to 2.1), 3 months (3.9 to 2.0), 6 months (4.0 to 2.2), 12 months (4.0 to 2.3) and 24 months (3.9 to 2.2), all p<0.0001.	Mean number of implants was 4.6 in RWR group	Within group A, 411 were catheterised post procedure as standard of care. Of the remaining 837, 133 (16%) were catheterised
Rubio et al (2019)			No significant differences found for IIEF a scores between baseline and 1 and 3 months follow-up.	Significant decrease in IPSS scores between baseline (18.94) and 1 month (13.77, p=0.003) and 3 months	Significant increase in Qmax between baseline (10.26) and 1 month (13.36) and 3 months (14.40), both p=0.003.		Mean operative time was 12 minutes Mean hospital stay was 4.5 h Mean number of implants used was	

				(11.28, p=0.001).			3.2	
Tutrone and Schiff (2020)			SHIM scores were significantly higher in the UroLift group (14.8) compared to Rezum (9.2), p=0.02. MSHQ-EjD scores were significantly higher in the UroLift group (12.2) compared to Rezum (9.2), p=0.04. There was no significant differences between groups for MHSQ-EjD bother scores.	IPSS scores were significantly higher in the Rezum group (15.6) compared to UroLift (8.6), p=0.001.		IPSS QoL scores were significantly higher in the Rezum group (2.5) compared to UroLift (1.5), p=0.04.		57% of UroLift compared to 87% of Rexum patients required post procedure catheterisation (p=0.03) Mean duration of catheterisation was 1.2 days for UroLift and 4.5 days for Rezum (p=0.0004)

6 Adverse events

Table 6 reports the full list of adverse events for all included studies. The reporting of adverse events was inconsistent between studies with some reporting full details using Clavien Dindo classifications and some reporting none at all. For those few studies that reported events but not using Clavien Dindo Classifications, the author compared the events listed to those within the Clavien Dindo classification to arrive at the correct Grade (Mamoulakis et al 2011; Ouattara et al 2019). These are marked with an asterisk within Table 6.

The severity of adverse events for this device are low with most events being Grade I or II including pain and discomfort, hematuria and one reported case of incontinence. However, one study did report several Grade IIIb events; severe bleeding and secondary treatment. Nothing above a Grade IIIb (i.e. severe) was reported.

The EAC identified 1 MHRA field safety notice which stated that upon implant deployment, the capsular tab may not be delivered as the needle is retracted. In this failure mode, the needle is deployed into the prostate and retracted, leaving no implant behind. Failure to deliver a capsular tab may result in a delay in completing a treatment or an inability to complete a treatment for the patient. Use of an affected device may lead to increased risk of existing adverse events associated with the product, including bleeding and tissue trauma associated with delivering the needle. It is important to note that this issue impacts only the delivery device with the UroLift implant itself not impacted. Any implants that have been delivered with the device are not affected. The company have added that this failure mode, which is likely due to improper deployment as a result of user error, is outlined in the Instructions For Use (IFU) that includes proper deployment technique and positioning guidelines.

Table 6: Adverse events

	Clavien Dindo classification system					
Study	**Grade I**	**Grade II**	**Grade IIIa**	**Grade IIIb**	**Grade IV**	**Grade V**
Roehrborn (2015)	Not graded: Peri-operative AEs were typically mild and transient, most frequently being hematuria, dysuria, pelvic pain, urgency, and urge incontinence.	Not reported	Not reported	Not reported	Not reported	Not reported
Sonksen (2015)	Total grade 1 AEs: Urolift n=30 patients (68%), TURP n=26 (74%), p=0.6. • Bleeding: UroLift n=17 patients (39% of patients), TURP n=20 (57%), p= 0.1. • Irritative symptoms, pain, or discomfort: UroLift n=23 (52%), TURP n= 21 (60%), p= 0.5. • Urinary incontinence: UroLift n=1 (2%), TURP n= 6 (17%), p= 0.04. • Urinary retention: UroLift n=4 (9%), TURP n= 0, p= 0.1.	Total grade 2 AEs: Urolift n=3 patients (7%), TURP n=4 (11%), p=0.7. • Urinary Tract Infection (UTI): UroLift n=3 (7%), TURP n=2 (6%), p>0.9 • Epididymitis: UroLift n=0, TURP n=2 (6%), p=0.2	None	• Bleeding: UroLift n=1 (2%), TURP n= 2 (6%), p=0.6 • Stricture: UroLift n=0, TURP n=1 (3%), p=0.4 • Secondary treatment: UroLift n=3 (7%), TURP n=2 (6%), p>0.9	Not reported	Not reported

	• Erectile dysfunction: UroLift n= 0, TURP n=3 (9%), p= 0.08. • Retrograde ejaculation: UroLift n=0, TURP n=7 (20%), p= 0.002. • Other: UroLift n=4 (9%), TURP n=3 (9%), p>0.9.					
Rukstalis (2016)	• Generally were mild to moderate and resolved within 0.5 months. No further details given. • 10 devices (4%) inadvertently deployed.					
Gratzke (2017)	Not reported.	Not reported	Not reported	Not reported	Not reported	Not reported
Bardoli (2017)	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
Roehrborn (2017)*	• UroLift: Hematuria n=1 • Urinary urge incontinence: UroLift n=1					
Rukstalis et al (2018)	Peri-operative adverse events were typically mild to moderate and transient, with the most frequent being hematuria and dysuria. Over the one-year course of the study, few related adverse events occurred after the first month.					

	No further details given					
Eure (2019)*	Not graded. Any adverse event: n=453 patients (66.8%). • Hematuria: n = 219 (17.5%) • Dysuria: n=83 (6.6%) • Incontinence: n=31 (2.5%) • Pelvic pain: n=23 (1.8%) • Urinary urgency: n=42 (3.4%) • Urinary frequency: n=16 (1.3%) There was a reported significant difference in number of adverse events between those treated in the clinic office (n=100) and those in other healthcare settings (n=353, p<0.0001).					
Rubio (2019)*	• Hematuria requiring catheterisation: n= 10 (50%). • Re-admission/re-operation with TURP: n=1 (5%))	• UTI: n=2 (10%)				
Sievert (2019)*	• Transient dysuria and haematuria: n= 12 (14.0%)					

	• Pelvic pain for less than a month: n=3 (3.5%)					
Tutrone et al (2020)	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
NHS Fife (2020)* **NICE SLCS**	• Urinary retention: n=2 • Temporary urinary urgency: n=6 • Haematuria but did not require an overnight stay: n=2	• Mild UTI: n=2				

7 Interpretation of the clinical evidence

Results from the evidence included in this report suggest UroLift is beneficial to patients compared to other procedures and across time. In relation to BPH symptom severity measures, BPH-II scores consistently improved over time and remained so up to 5 years post procedure (Roehrborn et al; 2015, Rukstalis et al; 2016, Roehrborn et al; 2017 and Rukstalis et al; 2018). The 2 studies comparing UroLift to TURP, however did not show any significant differences in amount of change in BPH-II scores between procedures across time (Sonksen et al; 2015 and Gratzke et al; 2016).

IPSS results indicated significant improvements in symptom severity compared to baseline for UroLift patients up to 5-years post procedure (Roehrborn et al; 2015, Bozkurt et al; 2016, Rukstalis et al; 2016, Bardoli et al; 2017, Roehrborn et al; 2017, Rukstalis et al; 2018, Sievert et al; 2018, Eure et al; 2019 and Rubio et al; 2019). However, when compared to TURP (Sonksen et al;2015 and Gratzke et al; 2016), patients who had undergone UroLift had significantly less improvement up to 12 months post procedure. When compared to Rezum (Tutrone and Schiff; 2020), IPSS scores was significantly better in UroLift patients approximately 30-days post procedure.

Changes in erectile and sexual dysfunction measures (MHSQ-EjD, IIEF and SHIM) varied between studies. The IIEF and SHIM questionnaires, (a shortened version of the IIEF) both focus specifically on erectile dysfunction. UroLift patients did not show significant improvements in these measures over time in the majority of studies (Roehrborn et al; 2015, Bozkurt et al; 2016, Rukstalis et al; 2016 and Rubio et al; 2019). However, Rukstalis et al (2018) looked specifically at OML patients and showed improvements in both of these measures up to 12 months follow-up. The amount of change in SHIM scores did not differ significantly between UroLift and TURP patients (Sonksen et al; 2015 and Gratzke et al; 2016). Tutrone and Schiff (2020) did however show that SHIM scores were better for UroLift patients when compared to Rezum, approximately 30 days post procedure. Scores for the MSHQ-EjD Function, which focuses on ejaculatory dysfunction as well as sexual health, were more consistent across studies. Out of 6 studies that reported MSHQ-EjD Function results, 3 showed that changes in scores over time were significantly better for UroLift patients when compared to TURP (Sonksen et al; 2015 and Gratzke et al; 2016) and Rezum procedures (Tutrone and Schiff; 2020). Roehrborn et al (2015) and Rukstalis et al (2016 and 2018) showed that following the UroLift procedure MSHQ-EjD scores significantly improved over time, compared to baseline, up to 3 years follow-up. One study however, showed no improvement over 12 months (Bozkurt et

al; 2016). Five studies reported MSHQ-EjD bother scores with 2 showing improvements over time (Roehrborn et al; 2015 and Rukstalis et al; 2018), 2 showing no significant differences between % improvement over time when compared to TURP (Sonksen et al; 2015 and Gratze et al; 2016) and 1 showing no significant difference between UroLift and Rezum patients at 30 days follow-up (Tutrone and Schiff, 2020).

Urological outcomes, PVR and Qmax, were measured in 11 of the 12 included publications. In the majority of studies, Qmax values improved over time for UroLift patients compared to baseline up to 5-years follow-up (Roehrborn et al; 2015, Bozkurt et al; 2016, Rukstalis et al; 2016, Roehrborn et al; 2017, Rukstalis et al; 2018, Sievert et al; 2018 and Rubio et al; 2019. Eure et al (2019) showed Qmax scores decrease over time up to 6 months follow-up, and Bardoli et al (2017) showed no significant differences across time. However, 2 studies showed patients who had undergone TURP had significantly bigger improvements in Qmax scores up to 24 months follow-up compared to UroLift (Sonksen et al; 2015 and Gratzke et al; 2016). Six studies reported PVR values, 4 of which showed a significant improvement up to 24 months for UroLift patients (Bozkurt et al; 2016, Rukstalis et al; 2016, Bardoli et al; 2017, Sievert et al; 2018). However, patients who had undergone TURP had significantly bigger improvements in PVR values compared to those who had UroLift (Sonksen et al, 2015 and Gratzke et al; 2016). Incontinence measures (ISI questionnaire) were only included in 2 studies; Sonksen et al (2015) showed significantly worse scores for TURP patients at 2 weeks and 3 months when compared to UroLift patients and Gratzke et al (2016) reports that ISI scores remained consistent for UroLift patients up to 2-years follow-up.

Eleven studies used QoL measures with 8 showing a significant improvement across time up to 5-years when using UroLift. When compared to Rezum, Tutrone and Schiff (2020) showed UroLift patients had significantly better scores at approximately 30 days follow-up. However, Sonksen et al (2015) and Gratzke et al (2016) showed no significant difference between scores in TURP and UroLift patients up to 12 and 24 months respectively.

One study comparing UroLift with TURP and another comparing UroLift and Rezum reported catheterisation rates were significantly reduced for UroLift patients. In addition, UroLift patients who were catheterised, were so for significantly less time, compared to both TURP (Sonksen et al; 2015) and Rezum (Tutrone and Schiff; 2020). Only the study comparing UroLift with TURP reported hospitalisation times which were also significantly reduced for UroLift patients. The studies just reporting on UroLift showed catheterisation rates from 0%-80% and hospitalisation times from 0.1-2 days (Roehrborn et al; 2015, Bozkurt et al; 2016, Rukstalis et al; 2018 and Eure et al; 2019).

When all three procedures; UroLift, TURP and Rezum are compared at a similar timeframe of 30days/1month using Tutrone and Schiff (2020) for Rezum and Sonksen et al (2015) for TURP, the results are again mixed. For symptom severity (IPSS), UroLift patients score best, followed by TURP then Rezum. SHIM scores show UroLift patients scoring highest, followed by TURP then Rezum and for the MSHQ-EjD, UroLift patients again score highest but followed by Rezum then TURP patients. Finally, for QoL scores, UroLift again scores best, followed by Rezum then TURP. As the Tutrone study does not compare to baseline the EAC cannot comment on the size of improvements but it would appear that UroLift patients are benefited from having this procedure for these outcomes at 1 month follow-up.

It should also be noted that the comparative results from Rukstalis et al; 2018 have not been discussed in full as the comparator is outside of scope. However, the results do show that UroLift is as beneficial for patients with OML in relation to symptom severity, ejaculatory and erectile dysfunction, urological and quality of life measures, when compared to LL patients from the L.I.F.T study.

In conclusion, the results are mixed and do not show that UroLift is superior when compared to TURP for urological, QoL or symptom severity outcomes. However, UroLift does appear to be superior to Rezum for erectile dysfunction and symptom severity outcomes. In addition, when looking at outcomes over time, UroLift does appear to improve patient's symptoms over a long timeframe. As the original assessment report (Ray et al, 2015) and UroLift guidance (MTG 26) did not include any comparison data, the results comparing with TURP and Rezum from this update cannot be compared. However, when looking at the results over time, the studies included in this update show a similar pattern of results i.e. improvements in symptom severity measures, urological outcomes and quality of life measures.

7.1 *Integration into the NHS*

Out of the 10 included studies (12 publications) only 2 were conducted wholly or partially in the UK. Therefore results from the evidence base as a whole are not fully generalisable to an NHS setting. However, there are six relevant NICE Shared Learning Case Studies (SLCS) (Table 7) which were done within the NHS using UroLift. Adverse events, BPH symptom severity measures, urological outcomes and sexual health outcomes were improved in all studies where they were reported. In one case study the use of either general or local anaesthetic was compared for the procedure, with no significant differences reported in terms of IPSS, QoL and pain scores post procedure.

Table 7 Results from abstracts and NICE SLCS

Study	Design	Key results
NHS Royal Devon and Exeter (2020)	A prospective database search of all patients undergoing Urolift. N=93 patients in total.	• Overall there were low complication and readmission rates in the patients treated with Urolift. • A few patients experinced haematuria and dysuria, but the majority back to normal activities, including work, within a week. • We have not seen any sexual side-effects, but have noted that some men have found that their sexual function has improved,
NHS Norfolk and Norwich (2019)	Audit data; • Jan 16-Sept 16 o UroLift n=72 o TURP n=122 o HoLEP n=115 • Jan 16 – June 19 o UroLift n=250 o TURP n=520 o HoLEP n=490	• At the 3 month follow-up, patients had significant improvements in the key clinical parameters, including IPSS, quality of life scores, urinary flow rate (Qmax) and post-void residual volume (RV) compared to TURP and HoLEP. • Between 80-85% of UroLift procedures are conducted under local anaesthetic with procedures taking on average, approximately half the time of TURP or HoLEP • Average length of stay for UroLift was 3-4 hours compared to 2.6-3 days for TURP and 16-17 hours for HoLEP.
NHS Fife (2020)#	61 men treated with UroLift who were eligible for TURP	• IPSS and Quality of Life scores were significantly improved in both groups, with no significant difference between the local anaesthetic (no anaesthetist) and general anaesthetic groups. • The 36 (85%) men who were sexually active had mean IIEF-5 score of 18 before and 18 after Urolift (range 16–18). • The mean pain VAS score was 2, and not significantly different between the LA and GA groups.
NHS Northampton January 2020	Retrospective comparison of Urolift,(n=20)_ and for TURP (n=20)	• Clinical results not reported • Operating time reduced from 45.3 min for TURP to 20.11 for Urolift • Length of inpatient stay reduced from 2.1 days for TURP to 0.27 days for Urolift.
NHS St Helens and Knowsley (2016)	Limited study details Urolift (n=7) biTURP (n=75) mTURP (n=17) HoLEP (n=6) TUIP (n=5)	• Clinical results not reported • Average length of stay for Urolift was day case and 1-2 days for all comparators • Estimated theatre time excluding 35 minutes induction and recovery (for all) was 10-30 minutes for Urolift, 30-75 minutes for biTURP, 30-60 minutes for mTURP, 60-120 minutes for HoLEP and 20-30 mintues for TUIP.
NHS Frimley park (2016)	Limited study details Urolift (n=75) TURis (n=190) Greenlight (n=80-90)	• Clinical results not reported • Urolift and Greenlight were carried out as day cases, TURis was carried out as inpatient. • Estimated theatre time was 25 minutes for Urolift, 60 minutes for TURis and Greenlight

***Data extracted from abstracts and NICE shared learning case studies cannot be critically appraised due to**

lack of included/relevant information

 # An abstract has been shared by the company at fact check, with the same results, accepted for publication (Société Internationale d'Urologie virtual annual congress 2020)

Only one of these case studies was comparative in design, and included limited information and therefore should be used with caution. However, all six suggest that UroLift is beneficial within an NHS setting, either on clinical or operational outcomes. Based on the above and operation/hospitalisation times reported in Table 5, if implemented widely throughout the NHS the rate of procedures for LUTS secondary to BPH conducted under local anaesthetic as a day case could increase, thus reducing hospitalisation time and associated costs.

The National Day Surgery Delivery Pack (Getting it right first time, 2020) identifies Urolift as being one of a number of procedures where the focus should be to develop an outpatient rather than day surgery pathway:

7.2 *Ongoing studies*

One relevant clinical trial was identified via clinicaltrials.gov.uk:

- NCT04338776 – Comparing UroLift experience against Rezum. Not yet recruiting.

Six other relevant trials were identified but had either finished recruitment or had withdrawn.

8 Economic evidence

8.1 *Published economic evidence*

Search strategy and selection

The company did not update their search strategy for the purpose of this assessment report (AR) update, however NICE conducted searches for an interim review of the guidance. These searches were based on the original AR searches and were completed on 31st July 2019. Please see Ray et al (2015) for critique of the original search strategies. To ensure that the EAC had access to all literature since the original assessment report was conducted, an updated search for this ARU was conducted. The searches detailed in 4.1 were for both clinical and economic evidence.

The submitted report does not refer to any economic evidence. The EAC identified 1 published cost effectiveness model (Ulchaker & Martinson 2018), 1 cost equivalence (DeWitt-Foy et al 2019) and 1 related review (Gill et al. 2018) that included cost information from the main literature search for the topic. All were set in the US.

Published economic evidence review

All three identified papers are based in the US making their findings of limited applicability. For this reason a full critical appraisal and data extraction have not been completed, instead the EAC have extracted relevant findings in the tables in Appendix D and described the model structure, assumptions and clinical inputs for background information.

The cost effectiveness model (Ulchaker & Martinson 2018) compares several procedures including Urolift, for treatment of symptoms due to BPH.

Most included adverse events are similar, but with the addition of erectile dysfunction, and an absence of TUR Syndrome and transfusion. These adverse events are split into early AE (occurring before 6 months) and late AE (after 6 months), with different probabilities.

The probability of adverse events and need for retreatment cannot be simply compared, as the published model reports a transition probability for a 6 monthly cycle, and the submission gives an absolute probability. However it is notable that the probability of retreatment is approximately 5 times higher than other procedures in the published papers, and only 3 times higher in the submitted model. For adverse events, Urolift has a 1% probability of incontinence per 6 month cycle in the papers, and a 0% probability in the submitted model.

When the initial procedure is either medical or minimally invasive treatment (MIT), then the first re-treatment is with MIT. If subsequent re-treatment is required, this is modelled using TURP or PVP (photoselective vaporization of the prostate).

Retreatment methods of MIT have an equal probability or being Urolift, Rezum or PVP.

Results from the economic evidence

The cost effectiveness study (Ulchaker & Martinson 2018) found that Urolift was dominated by Rezum, being more expensive and less effective. The cost equivalence study found Urethral Lift to be more expensive to provide than any of the other techniques considered except open or robotic prostatectomy (De Witt –Foy et al. 2019). These studies were not included in the company submission, and they are not of direct relevance as they are set in the US. De Witt-Foy note that their results are very different from studies in Europe for TURP and medication, and differences are likely to be apparent across all therapies.

8.2 *Company de novo cost analysis*

The company submitted a de novo model in Treeage, broadly based on the previously submitted model used for the MTG26 guidance (2014), which was in Excel. The company have added Rezum as a comparator, and also included median lobe treatment using Urolift.

Due to changes in costing methodology, naming of variables, different software the models look visually very different and calculations are structured in a different way. However beyond this, the essential decision tree is similar.

The costing of elements has changed to include less detail, meaning that where the original model had taken the different elements of a complication cost and priced each individually the new model prices them as a lump sum.

The new model includes branches for success (symptom relief) or failure, and both branches may be with or without incontinence.

Patients with first treatment failure may have no symptom relief and no incontinence, in which case they are scheduled for re-treatment. Patients with no symptom relief and incontinence receive no more treatment for LUTS.

Patients modelled as experiencing incontinence receive an annual cost of incontinence management including incontinence products and pharmaceutical treatment. This is added for the duration of the model.

The second treatment chosen is dependent on the initial treatment, but may include alternative technologies. For any one technique, the probabilities of success or complications are the same for first and second procedures.

The new model has the time horizon extended from 2 to 5 years, with the following elements are affected by the time horizon are:

- the cost of incontinence over that period
- the rate of failure selected for Urolift (this is a fixed rate within the model, but dependant on the time horizon chosen)

There is no Markov element included in the model, no discounting and no consideration of mortality. The original model (MTG26) included 3.5% discounting for a 2 year time horizon.

Economic model parameters

The EAC have updated all costs to 2019 values, and used the submitted model as the base case with minor changes that are noted in subsequent sections. Scenario analyses are presented to highlight the difference in assumptions between this model and that submitted previously for MTG26.

Clinical parameters and variables

Clinical parameters have been added for Rezum as this is a new comparator since previous guidance in 2014. The clinical parameter values are based on McVary et al., 2016 and were accepted in the recently published MTG49 (2020).

Clinical parameters for Urolift are based on the LIFT trial, using 5 year data (Roehrborn 2017). MTG26 was based on clinical parameters from the same trial at one and two years (Roehrborn 2013, 2014).

Adverse events and failure rates

Clinical parameters for TURPs and HoLEP technologies are based on the HTA by Lourenco et al. 2008, and were also used for MTG26, MTG29 and MTG49. The values are based on 12 months of data, which the EAC accept as reasonable for adverse events which are most likely to occur close to the procedure time. Failure rates are defined as less than 10% improvement in IPSS scores, and are modelled as requiring repeat procedures, if there is no incontinence. It is possible that longer term failure rates may vary. In addition,

over the last 12 years techniques may have improved to reduce adverse event rates for the comparator procedures. The EAC have accepted these values, as they have been used in other recent guidance, however future reviews may need to consider if there is a need to update these sources.

The clinical parameters used in the submitted model are presented in table 8. It should be noted that there are some discrepancies in Lourenco et al. 2008 that were noted by the EAC in MTG29, and have now been corrected in the HTA and the current model.

HoLEP failure rates at 12 months were calculated in the original model based on relative IPSS scores (Lourenco 2008), however this did not contribute to overall cost calculation The figure of 4.1% used in the current model is taken from Lourenco 2008, table 30.

Table 8: Clinical parameters used in the company's model and any changes made by the EAC

Original submitted model: probability of failure or complications							
	Failure	Incontinence	Retention	Stricture	Transfusion	TUR Syndrome	UTI
Urolift	10.9%	0.0%	6.0%*	0.0%	0.0%	0.0%	1.4%
rezum	n/a	n/a	n/a	n/a	n/a	n/a	n/a
mturp	6.0%	3.00%	5.0%	7.0%	8.0%	3.0%	6.0%
bi turp	6.0%	1.77%	8.6%	9.7%	8.2%	3.0%	6.0%
holep	3.3%*	2.91%	3.6%	5.9%	2.2%	0.9%	5.9%
Updated submitted model: probability of failure or complications							
	Failure	Incontinence	Retention	Stricture	Transfusion	TURS	UTI
Urolift	13.6%	0.0%	0.4%	0.0%	0.0%	0.0%	0.1%
rezum	4.4%	0.0%	0.5%	1.1%	0.0%	0.0%	2.1%
mturp	5.8%	3.0%	3.8%	7.0%	8.0%	3.0%	6.0%
bi turp	5.8%	3.0%	3.8%	7.0%	8.0%	3.0%	6.0%
holep	4.1%	2.9%	3.6%	5.9%	2.2%	0.9%	5.9%

Abbreviations: TUR: Transurethral resection, TWOC: Trial without catheter, UTI: Urinary Tract Infection
*There is no cost attached to this probability, therefore it is effectively 0% in the model

Repeat procedures

Both MTG26 and MTG49 have accepted the assumption that for HoLEP there was no re-treatment following failure and therefore failure rates did not contribute to the overall cost calculation. The current submitted model assumes that there is treatment possible following failure of HoLEP, and this

increases the cost of HoLEP, as the total number of procedures carried out increases. Expert advice during the recent MTG49 guidance was that retreatment would be rare, and therefore the EAC have removed the possibility of retreatment following HoLEP. This has been done by setting the failure rate at 0% in the model.

Assumptions for repeat procedures have changed significantly, as shown in table 9. In the original model all patients who had retreatments received either monoTURP, or,if they had been initially treated with biTURP, retreatment with biTURP. Patients treated with HoLEP did not receive second treatments.

Table 9 Retreatment methods for original and updated models

Original submitted model (MTG26, 2014): method of retreatment					
Repeats	**Urolift**	**rezum**	**mturp**	**bi turp**	**holep**
Urolift	0	n/a	1.0	0	0
rezum	n/a	n/a	n/a	n/a	n/a
mturp	0	n/a	1.0	0	0
bi turp	0	n/a	0	1.0	0
holep	0	n/a	0	0	0
Submitted model (2020): method of retreatment					
Repeats	**Urolift**	**rezum**	**mturp**	**bi turp**	**holep**
Urolift	**0.31579**	**0**	**0.171053**	**0.513158**	0
rezum	**0**	**0.5**	**0.125**	**0.375**	**0**
mturp	0	0	**0.25**	**0.75**	0
bi turp	0	0	**0.25**	**0.75**	0
holep	0	0	**0.25**	**0.75**	0

In the updated model, for all repeat procedures that are carried out with TURP there are 75% biTURP and 25% mTURP. This is the same assumption as accepted in MTG49, based on expert opinion that biTURP procedures are now more prevalent than mTURP. For Rezum, 50% of repeat procedures use Rezum, and 50% use TURP, based on the company submission for MTG49. During assessment of the model for MTG49 the EAC changed this proportion to 40% retreated by Rezum, which would increase the cost of Rezum treatment slightly. This change was based on outcomes for 6 patients, and the EAC have accepted the submitted model values as submitted as a more conservative assumption.

Where first treatment is with Urolift, approximately 32% of repeat procedures use Urolift and the remainder use TURP, this was accepted for MTG49 and is appropriate for use in this model. The data is from the 5 year LIFT study (Roehrborn 2017). Repeat procedures are modelled as having the same success rate as initial procedures.

Resource identification, measurement and valuation

The cost parameters are mainly based on the original model as accepted in MTG26 guidance, with additional information from guidance in MTG29 and MTG49. In some instances although previous guidance has been quoted, the actual costs, or the way in which they are used, is not the same. Where this is the case the EAC have highlighted this. Table 10 includes the original parameters accepted in MTG26, the current submitted model and current EAC values. The EAC have updated costs to 2019 where relevant and used these in the EAC base case. Where alternative values have been suggested these are used in the sensitivity analysis scenarios.

Follow up costs

In addition to table 10, it is worth noting that follow up costs have been changed to vary between different technologies, as shown below:

Urolift	Telephone consultation, 20 min with nurse	£15.70
Rezum	Outpatients appointment with consultant plus trial without catheter (TWOC)	£238
BiTurp, MTurp, HoLEP	Outpatients appointment with consultant	£94

Device costs

Capital costs have been removed from the current model, this has very little impact on the overall result

Consumables costs have been updated to 2019, and in addition the costs for mTURP and biTURP now include additional items based on calculations in MTG29 and MTG29. There is some variation between the guidance documents on how these calculations should be interpreted. The EAC have

changed the submitted company model parameter to be inline with the accepted calculation method in MTG49.

Costs removed from the model

The model used in MTG26 also included costs for :

- Pre procedure outpatients consultation
- Pre and post procedure tests
- Fluids and other consumables during procedures

these were the same for all procedures, so removing them is appropriate and reduces costs for all procedures equally.

Table 10: Cost parameters used in the company's model and changes made by the EAC

Description	Original Value	Original Source	Submitted Value	Source	EAC update	
Cost of Adverse Events						
AUR treatment (c_compRet)	£2, 683	Annemans 2005	£3,061.79	Rezum Medical Technology Guidance 2020 (MTG49) – Inflated to 2019 from Annemans 2005	**£3,061.79**	No change
Stricture (c_compStric)	£550.99	54% at £373.60 day case, NHS National Schedule of Reference Costs, 2013-14.TDC. Code LB15E, Minor Bladder Procedures, 19 years and over 46% at £759.23, inpatient NHS National Schedule of Reference Costs, 2013-14. EI. Code LB15E, Minor Bladder Procedures	£504.84	**68% at £309;** NHS Ref costs 2017-18; Day case HRG LB15E Minor bladder procedures, 19 years and over + **32% at £921** NHS Ref costs 2017-18; Elective inpatient HRG LB15E Minor bladder procedures, 19 years and over.	**£520.40** using 68% / 32% split. [Using 54% : 46% split would give £596.70]	Updated costs using NHS Ref costs 2018-19. The EAC have used the submitted %, but highlight that it has not been justified by the company. In previous guidance MTG49 the cost was £330, There is no explanation given for why these have changed. MTG49 Rezum used £330 which is the total HRG average cost for NHS ref costs 2017-18
Transfusion (c_compTrans)	£329	£121.85 per unit RBC NHS price list 2014/15, 2.7 units. Used in EAC base case (original model used £862, NICE 2010)	£348	Updated cost from MTG26 [Actually included in submitted mode as £357.95]	**£348**	£128.99 per unit RBC NHS price list 2018/19, 2.7 units. This is in line with previous accepted costs, but does not include costs of delivering the transfusion.
TUR (c_compTURS)	£1,875.36	2 days in high dependency ward (£643.00) CCSALCCU. Code XC07Z, Adult Critical Care, 0 Organs Supported and 2 days in normal ward (294.36)EI_XS. Code LB25F,	£2,102	2 days in high dependency ward (£693.00) and 2 days in normal ward £358.00 NHS reference costs 2017-18	**£2,500**	Update using NHS Ref costs 2018/19: £883 for 2 days, XC07Z Adult critical care. £367 for 2 days, normal ward, inflated to 2019 from £358 as

		Transurethral Prostate Resection Procedures with CC Score 0-2 NHS reference costs 2013/14					reference cost no longer available.
UTI_(c_compUTI)	£47.48 for Urolift	1	£45.64, GP visit PSSRU 2014	£781	Updated from MTG26 NHS reference costs 2017/2018 LA04S	**£738** updated model, 2018/19 NHS Ref costs [Alternative: £935.6]	Updated model assumes same cost for both Urolift and comparators, which is conservative compared to previous model. Uses total HRG for LA04S, NHS ref costs 2018/19 If using costings from original model, this would be: 0.9 x £257 LAO4S, day case 0.1 x £1,011 LA04M, NEI-short stay (NHS Ref costs 2018/19)
		1	£1.84, 10 days antibiotic BNF 2014				
	£709.14 for other procedures	0.1	£367.69, NHS Ref Cost 2013/14 LA04G UTI 1 day				
		0.9	£747.08, NHS Ref Cost 2013/14 NEI-Short stay. Code LA04M				
Incontinence (c_incont) (per year)	£2,425.57, year 1 £2,184.55, year 2	Complex calculation with 95% of patients receiving medication plus incontinence products, 5% of patients treated with AUS implant.		£2,356.97	Inflated cost from MTG26; used in Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation	**£2417.47 per year** **For 5 years =** £12,087.35 With 3.5% discount = **£10,641.84**	Submitted costs are inflated from original model. EAC inflated to 2019 to give £2417.47, or £12,087.35 Scenario using discount at 3.5% for 5 years using CPI Health Index.
Device capital costs per procedure							
Urolift	£2.50	£5,199 with 250 uses per year over 10 years		£0	Device is free of charge with consumables contract	No change	
Rezum	n/a			£0		No change	
TURP	£0	Equipment assumed already available		£0		No change	

HoLEP	£80.59	£167,555 with 250 uses per year over 10 years	£0		No change	
Procedure consumables						
Number of Urolift devices used per procedure (DevicesUsed)	4		3.5	Source: Data on file. [redacted] collected from NHS trusts [redacted]; [redacted] Also verified by local audits carried out by NHS users [NHS Fife 2020; [redacted]; [redacted]; Royal Devon & Exeter NHS Trust 2020; Norfolk & Norwich NHS Trust 2019]	No change	
Urolift device, each (c_deviceprice)	£330.00	Neotract	[redacted]	Manufacturer provided	<u>No changes</u>	
Bipolar TURP consumable (c_consumablesBTURP)	£52.50	NICE 2010, clinical expert opinion (assumed same as MTURP)	£256.74	Source: NICE MTG 29 Greenlight Laser Bi-TURP includes: • 1 Bi-Loop per surgery, unit cost £189.34 plus 4 bags of glycine fluid, unit cost of £5.34, plus 0.5 roller ball3333333 pieces per surgery, unit cost £50 • 1 Ellik evacuator per patient, unit cost £21.04 • No capital or servicing costs	**£226.86**	Figure does not appear in any guidance or supporting docs, but method taken from MTG29 and MTG49. Figure used is manufacturer submission MTG49. Does not include glycine or roller ball. Taken individual prices from 2016 and inflated to 2019 using CPI Health. Glycine and roller ball not included, in line with MTG49 Prices for TURP consumables were based on expert opinion in 2016 and have been

						interpreted differently between guidelines.
HoLEP consumable (c_consumablesHoLEP)	£664.63	NICE 2010, SIGMACON supplier	£448	Blended technology cost used in Rezum Medical Technology Guidance 2020 (MTG49) – Supporting Documentation	No change	
Monopolar TURP consumable (c_consumablesMTURP)	£52.50	NICE 2010, clinical expert opinion	£88.44	From NICE MTG29 for Greenlight laser Mono-TURP includes: • 1 Mono-Loop per surgery, unit cost £52.60, plus 4 bags of glycine fluid, unit cost of £5.34, plus 0.5 roller ball pieces per surgery, unit cost £50 • 1 Ellik evacuator per patient, unit cost £21.04 • No capital or servicing costs	**£129.40**	As above for BiTURP, including all items listed by company, in agreement with MTG49.
Rezum single use treatment set (C_consumablesRezum)		Not included as comparator in original model	£1,348	Rezum Medical Technology Guidance 2020 (MTG49)	No change	
Staff Costs						
Anaesthetist (per min)	£1.65	£99 per contact hour, PSSRU 2013	£1.82	PSSRU 2019. Table 14. Hospital-based doctors. Cost per hour = £109	No change	
Band 5 nurse (per min)	£1.40	£84 per contact hour, PSSRU 2013	£1.53	PSSRU 2019. Table 13. Hospital-based nurses. Band 5 nurse. Cost per hour patient contact = £92	No change	

Healthcare assistant (per min)	£0.35	£21 per hour, PSSRU 2013	£0.36	Urolift update. EAC used £21.40 per hour (p7 of 15). Band 2 costs not available in PSSRU	**£0.37**	Inflated to 2019
Surgeon (per min)	£1.65	£99 per contact hour, PSSRU 2013	£1.82	PSSRU 2019. Table 14. Hospital-based doctors. Cost per hour = £109	No change	
Other procedure costs						
Inpatient stay (per day) (c_LOS_hospital)	£344	Excess bed day cost is calculated from the HRG code for TURP, minus the procedure costs included in the model	£370.32	Accepted cost in Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation	**£365**	Cost given in Rezum EAC AR 2019.
Number of extra Urolift implants: obstructive median lobe (c_medianLobe)		Not included in original model	1.3	Number of extra implants used in Medlift study [Rukstalis 2019]	No change	No change
Operating theatre per min (c_room_theatre)	£5.23	NICE CG97 Urology operating theatre cost of £9 per minute inflated to 2014, costs subtracted for staff time.	£14	PLICS 2016-17 https://analytics.improvement.nhs.uk/t/Public/views/PLICSPublicViewPrototype2016-17data/CostofNHSservices?iframeSizedToWindow=true&:embed=y&:showAppBanner=false&:display_count=no&:showVizHome=no	**£14.60**	EAC: ISD Scotland cost book 2019, average hourly cost for theatres (urology) includes staff
Follow up costs						
Outpatient consultant consultation (c_visit_OPconsultant)	£99.16	NHS National Schedule of Reference Costs, 2013-2014. Table OPATT,	£112	National Schedule of Reference Costs 2017/18; Urology O/P - consultant led	**£110**	Total outpatient attendances, Urology, consultant led. NHS Ref costs 2018/19
Outpatient nurse consultation (c_visit_OPnurse)		Not included in original model	£94	Source: National Schedule of Reference Costs 2017/18; Urology O/P - non-consultant led	**£88**	Total outpatient attendances, Urology, non-consultant led. NHS Ref costs 2018/19

nurse led telephone consultation (c_visit_telephoneconsult)		Not included in original model	£15.7	Estimate based on 20 mins specialist nurse (Band 6). £47/hour. Source: Unit Costs of Health and Social Care. Personal Social Services Research Unit 2019	**£37.67**	20 mins specialist nurse (Band 6). £47/hour. PSSRU 2019 OR £113 patient facing hour
Outpatient visit for a trial without catheter (C_visit_TWOC)	£316.23	NHS National Schedule of Reference Costs, 2013-14. OPPROC, code: EA36H Catheter with CC score 0-1' (none actually included in original model)	£144	Procedure code OPCS M47.3 Removal of urethral catheter from bladder. Maps to HRG LB15E. National Reference cost (2017/18) – Outpatient procedure (OPROC): £144	**£135**	HRG LB15E. National Reference cost (2018/19) – Outpatient procedure (OPROC)

Resource use parameters

Length of stay post procedure (days)						
bipolar TURP (LOS_BTURP)	2.63		2.33	Source: Original NICE Guidance (EAC report p75). Same LOS was used in the more recent Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation	**2.63**	This is the figure in the manufacturer submission and used in the model. Lourenco et al. 2008. Possibility that biTURP can now be done as day surgery (expert opinion from PLASMA update) this would reduce LOS – explored in scenario.
HoLEP (LOS_HoLEP)	1.98		1.98	Source: Original NICE Guidance (EAC report p75). Same LOS was used in the more recent Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation	No change	Lourenco 2008

MonopolarTURP (LOS_MTURP)	3.03		3.03	Source: Original NICE Guidance (EAC report p75). Same LOS was used in the more recent Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation	No change	Weighted average of HRG4 codes LB25A, LB25B, LB25C (HSCIC 2013)
Urolift (LOS_PUL)	0.5		0.125	This LOS was agreed and used in the final base case for the Urolift NICE guidance (MTG26; pages 11 and 92 https://www.nice.org.uk/guidance/mtg26/documents/urolift-for-treating-lower-urinary-tract-symptoms-of-benign-prostatic-hyperplasia-assessment-report2). This length of stay (routinely 3 hours) has been confirmed in numerous reports from NHS hospitals. This LOS was also used by the EAC for the day case scenario in the recent Urolift guidance review (p11 of 15)	No change	Used for day case scenario. All routes are day patient or clinic in
Rezum (LOS _Rezum)			0.5	Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation	**0.5** [Alternative would be 0.125]	Rezum submission was based on equivalence to Urolift. Therefore scenario modelled using 0.125, same value as Urolift.
Theatre time (minutes)						

bipolar TURP (theatretime_BTURP)	55.44	.	66	Source: Original NICE Guidance (EAC report p75). Same procedure time was used in the more recent Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation (p126-127)	**55.44**	In MTG26 the EAC updated mTURP to 66 minutes, but BiTURP was unchanged at 55.44 minutes
HoLEP (theatretime_HOLEP)	79.96		80.2	Source: Original NICE Guidance (EAC report p75). Same procedure time was used in the more recent Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation (p126-127)	**79.96**	This is the value stated in EAC assessment report p75, and used in the model. There will be minimal difference in the result.
monopolar TURP (theatretime_MTURP)	66		66	Source: Original NICE Guidance (EAC report p75). Same procedure time was used in the more recent Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation (p126-127)	No change	
Urolift procedure (theatretime_PUL)	30	30 minutes in submitted model, EAC calculated weighted average of 60 minutes	14	Source: Data on file. [redacted] collected from NHS trusts [redacted]. Details supplied separately; [redacted]	No change	Accept change of practice and new data. Note that MTG49 Rezum used 30 min based on clinical advice.
Rezum procedure (theatretime_Rezum)		Not included in original model	17.5	Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation	No change	

Table 11 summarises the setting, number of participants, length of stay and procedure time for Urolift for each of the included studies, and the NICE shared learning case studies for NHS implementation. It should be noted that none of the studies gave a clear definition for procedure time and there is likely to be a difference between theatre time and anaesthesia time as shown in Bardoli et al (2017). These results are presented in more detail in the clinical section (tables 3,4 and 7), including additional information for comparators where available.

Table 11 Length of stay and procedure time for Urolift

Study	Setting	N Urolift	Length of stay (days)	Procedure time (minutes)
Roehrborm et al (2015) L.I.F.T study	USA Canada Australia	140	0.19	66.16 procedure time.
Sonksen (2015) The BPH6 study.	Denmark UK Germany Italy	45	1	55 minutes Anaesthesia time
Bozkurt (2016)	Turkey	17	<1 day	29.1 minutes operation time.
Gratzke et al (2016) The BPH6 study.	Germany UK Denmark	45	Not reported	Not reported
Rukstalis et al (2016) L.I.F.T study	USA Canada Australia	51	0.21 days	51.25 Anaesthesia time
Bardoli et al (2017)	UK	11	10.6 hours (0.44 days)	8.5 minutes operation time. 18.7 minutes theatre time
Roehrborm et al (2017) L.I.F.T study			Not reported	Not reported
Eure et al (2019)	USA Australia	1413	Not reported	Not reported
Sievert et al (2019)	Germany	86	2.0 days	57 minutes operation time
Rubio et al (2019)	Spain	20	4.5 hours (0.1875 days)	12 minutes operative time.
Tutrone and Schiff (2020)	USA	53	Not reported	Not reported
NHS Norfolk and Norwich (2019)	UK	322	3-4 hours (0.125 – 0.167 days)	25 minutes
NHs Northampton	UK	20	0,27 days	20.11 minutes operating time
NHS Frimley Park	UK	75	Day case	25 minutes
NHS St Helens and Knowsley Teaching Hospital	UK		Day case	10-30 minutes (excluding 35 minutes induction and recovery time)

NHS Fife	UK	42	Not reported	17 minutes
NHs Royal Devon and Exeter	UK	93	Not reported	Not reported

Sensitivity analysis

The company provided one way sensitivity analysis for the number and price of Urolift devices, the number of additional devices required for median lobe treatment, the proportion of treatments for median lobe and the incidence of UTI with Rezum.

The company also completed probabilistic sensitivity analysis showing that Urolift with no anaesthetist was the cheapest option in 59.4% of 10,000 model iterations.

The EAC updated one way sensitivity analysis using the EAC base case, and added additional variables to the analysis as well as additional scenarios:

- LOS for Rezum is 0.125 days
- All follow-ups by telephone consultation, for all comparators
- BiTURP has day surgery, using LOS =0.5 days
- Remove staff costs from theatres – there is an element of double counting in the costs used.
- Alternative increased costs for UTI
- 1% for Rezum and Urolift for incontinence, based on MTG49 assumption
- Theatre time for Urolift is 30 min, based on previous guidance (MTG26)

These scenarios should be seen as explorations of the assumptions made, rather than preferred results.

8.3 *Results from the economic modelling*

Impact of EAC changes

The EAC have updated costs to 2019 values as shown in table 12. In addition the EAC base case makes the following changes:

- Addition of 3.5% discounting for the cost of incontinence over 5 years
- Removal of second procedures following HoLEP
- Length of stay and theatre times for comparators changed to those in original submitted model (MTG26)

Table 12 EAC changes to model with impact

Variable	Out	Day	Rezum	BiTURP	MTURP	HoLEP
Company base case	**2240.414**	**2264.62**	**2305.564**	**3296.903**	**3387.827**	**3542.552**

	24.206	*0*	*-40.9441*	*-1032.28*	*-1123.21*	*-1277.93*
All costs updated according to table in AR	2284.116	2308.322	2305.472	3430.084	3478.619	3593.92
	24.206	*0*	*2.84949*	*-1121.76*	*-1170.3*	*-1285.6*
HOLEP failure = 0	2284.116	2308.322	2305.472	3430.084	3478.619	3474.9
	24.206	*0*	*2.84949*	*-1121.76*	*-1170.3*	*-1166.58*
discounting added - use 10641.84/5	2280.089	2304.295	2304.509	3384.279	3432.815	3432.835
	24.206	*0*	*-0.21362*	*-1079.98*	*-1128.52*	*-1128.54*
theatre times updated	**2250.466**	**2274.672**	**2297.419**	**3165.618**	**3414.869**	**3428.002**
	24.206	*0*	*-22.7474*	*-890.947*	*-1140.2*	*-1153.33*

Base case results

Table 13: Summary of base case results

	Original guidance		**Submitted update (2020)**		**EAC base case (2020)**	
Scenario	Per patient cost	Incremental cost vs. Urolift	Per patient cost	Incremental cost vs. Urolift	Per patient cost	Incremental cost vs. Urolift
Urolift – Outpatient	n/a	n/a	£2,240	£ -	£2,250	
Urolift – day case	£2,405	£ -	£2,265	£24	£2,275	£24
Urolift - inpatient	£2,979	£574	n/a	n/a	n/a	*n/a*
Rezum	n/a	n/a	£2,306	£66	£2,297	£47
BiTURP	£2,564	£159	£3,297	£1,057	£3,166	£915
MonoTURP	£2,691	£286	£3,388	£1,148	£3,415	£1,164
HoLEP	£2,315	-£90	£3,543	£1,303	£3,428	£1,178

The submitted model has reduced the cost of Urolift provision compared to the original guidance (MTG26, 2015). The key elements of this cost reduction come from:

- Reduction of devices per implant from 4 to 3.5 (reduction of £200, based on submitted audit data) (most included studies are 4+)
- Reduction of time in theatre from 30 minutes to 14 minutes (reduction of £322.24, based on submitted audit data)

  Change to telephone consultation for follow-up (Urolift only) (reduction of £72.33 – using EAC values of £37 for patient facing nurse time)

In addition the submitted update has increased the cost of BiTURP, MonoTURP and HoLEP compared to the original guidance (MTG26, 2015). The key elements of this cost increase, in addition to inflation come from:

- Increase in consumables costs for biTURP, and to a lesser extent for o monoTURP.

- Increased impact of incontinence due to change in calculations between models.

In the model for MTG26 guidance, the incontinence rates were applied only to patients where treatment had failed. In the current submitted model the incontinence rates are applied to the whole population who have treatment

The model can also be compared to that submitted for MTG49 Rezum (2020), in which Rezum was cost saving compared to Urolift. Both models took many variables and model structure from both MTG26 Urolift and MTG29 Greenlight.

The key changes in the current submitted model for Urolift, compared to MTG49 are:

- Reduced change in theatre time for Urolift from 30 to 14 minutes (included studies are between 8min and 1 hour, 4 are closer to an hour)

- Reduced length of stay for Urolift from 0.5 days to 0.125 days.

- Change to telephone consultation for Urolift.

- Additional trial without catheter (TWOC) appointment for Rezum (was included in some EAC scenarios for MTG49)

MTG49 guidance accepted a value of 0.5 days for both Urolift and Rezum for the length of stay. This was based on the value of 0.5 days for one of the scenarios in MTG26, and an assumption that the length of stay for Rezum would be equal to Urolift.

in MTG49 was assumed to be the same as Urolift at 0.5 days. In the current model, Resum remains at 0.5 days, but Urolift is 0.125 days as in the accepted guidance for day case surgery. If both were set at 0.125, Rezum would be cost saving compared to Urolift.

Sensitivity analysis results

Additional Scenarios presented by EAC

The EAC calculated scenarios for the following scenarios, shown in table 14.

The first scenario included is for a reduced LOS for Rezum (0.125 days, or 3 hours) based on an assumption from MTG49. There is no evidence to support this reduced length of stay, the scenario is intended to explore the uncertainty. HES data submitted by the company during fact check indicates a length of stay of 0.87 days, however there absence of a specific code for use of Rezum reduces confidence in this figure. No data for length of stay was identified for Rezum during MTG49.

The third scenario sets biTURP length of stay at 0.5 days (or 12 hours) to explore the impact of biTURP being carried out as a daycase procedure.

Included data and NHS patient information (NHS website) point to around 2 days being a typical length of stay currently, however there is evidence that it can be carried out as a daycase for some patients within the NHS (Lavan 2018). This scenario explores the potential impact if this were to become more widespread.

Table 14 Impact of EAC Scenarios	
Scenario	**Impact**
LOS for Rezum is 0.125 days	Urolift no longer cost saving compared to Rezum
All follow-ups by telephone consultation, for all comparators . An additional TWOC appointment remains in place for Rezum.	Reduction in costs for all comparators, Urolift no longer cost saving compared to Rezum
BiTURP has day surgery, using LOS =0.5 days	Reduction in costs for all technologies except HoLEP, Urolift remains cost saving compared to all.
Remove staff costs from theatres – there is an element of double counting in the costs used.	Reduction in costs for all technologies. Urolift remains cost saving compared to all.
Alternative increased costs for UTI	Minor difference. Urolift remains cost saving compared to all.
1% for Rezum and Urolift for incontinence, based on MTG49 assumption	Increased cost for Urolift and Rezum, Urolift remains cost saving compared to all.
Theatre time for Urolift is 30 min, based on previous guidance (MTG26)	Urolift no longer cost saving compared to Rezum

One-way sensitivity analysis

The EAC repeated the company's sensitivity analysis with the updated EAC base case, and also considered additional variables as shown in table 14. It should be remembered that each result changes only one variable at a time.

Table 15 One way sensitivity and threshold results

Variable changed	**Range**	**Threshold**		**Description**
		company	**EAC**	
Number of Urolift devices	3-6	3.65	3.61	Rezum is cheaper option if over threshold
Price of Urolift devices	350 – 425	£417.55	£412.65	Rezum is cheaper if over threshold. [redacted], but the current list price [redacted] per device.
Additional devices for treating median lobe	0-3	-	-	Urolift remains cheaper

Probability of hyperplasia being present in the median lobe	0.02-0.2	0.178	0.143	Rezum is cheaper if probability is greater than threshold
Incidence of UTI with Rezum	0.02-0.17	-	-	Urolift remains cheaper [Company submission: cost of Rezum increases to £2,421 at 17% (upper range from Mollengarden 2018)]
Theatre time Urolift	10 - 30	NA	16.70	Urolift cost saving if theatre time for Urolift < threshold
LOS Rezum	0.1-0.5	NA	0.374	Rezum cost saving if LOS < threshold
LOS Urolift	0.1-0.5	NA	0.248	Urolift cost saving if LOS < threshold
Cost of follow up consultation, Urolift	15.7 - 110	NA	£87.09	Urolift cost saving if followup <threshold. This is less than cost for other procedures.
LOS BiTURP	0.5-2.63	NA	-	Urolift remains cost saving, although BiTURP approaches values for Rezum and Urolift when LOS BITURP=0.5 days
Theatre time Rezum	0-17.5	NA	15.17	Urolift is cost saving where theatre time for Rezum > threshold

For selected key variables, threshold graphs are shown (figures 1 to 5). Figure 1 demonstrates the strong dependence of the model results on the theatre time required for Urolift. Figure 2 shows that lower lengths of stay for Rezum could result in Rezum becoming cost saving. Figure 3 demonstrates that if bipolar TURP were to move to day surgery, the reduced length of stay would have a large impact on the overall cost of the procedure. However, when considering only this one change, it would be unlikely to become cost saving compared to Rezum or Urolift.

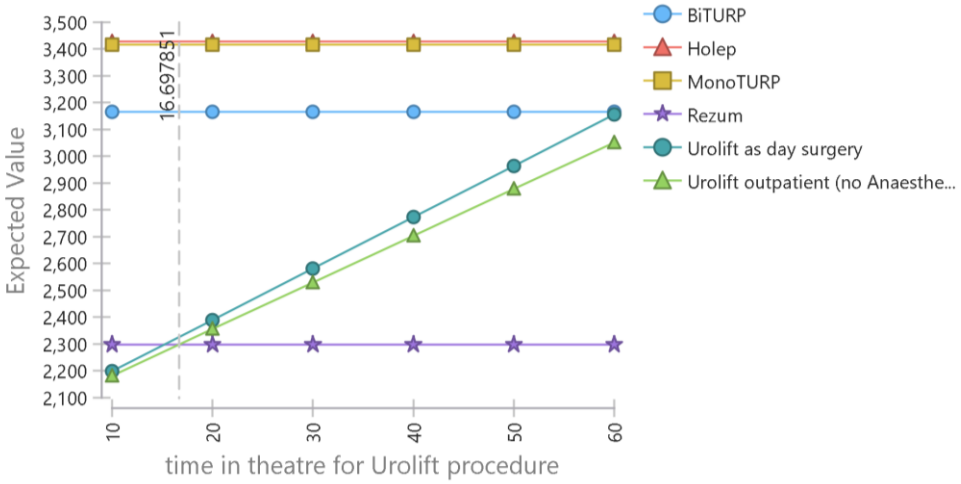

Figure 1One way sensitivity analysis for Urolift time in theatre

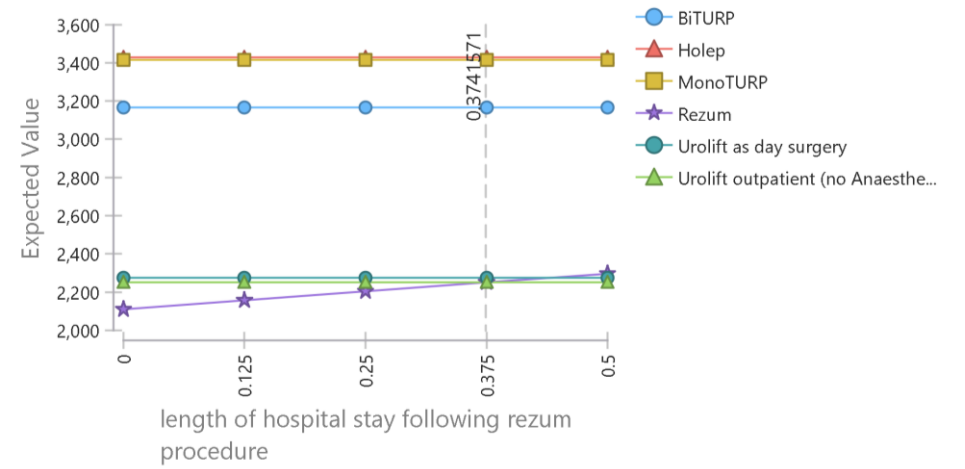

Figure 2 One way sensitivity analysis for length of hospital stay following Rezum

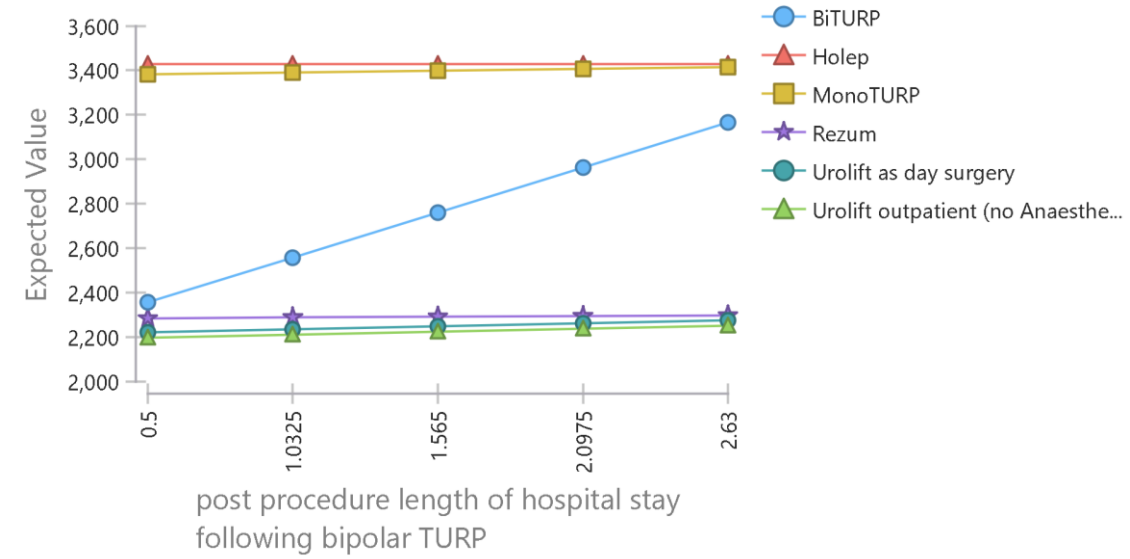

Figure 3One way sensitivity analysis for length of hospital stay following bipolar TURP

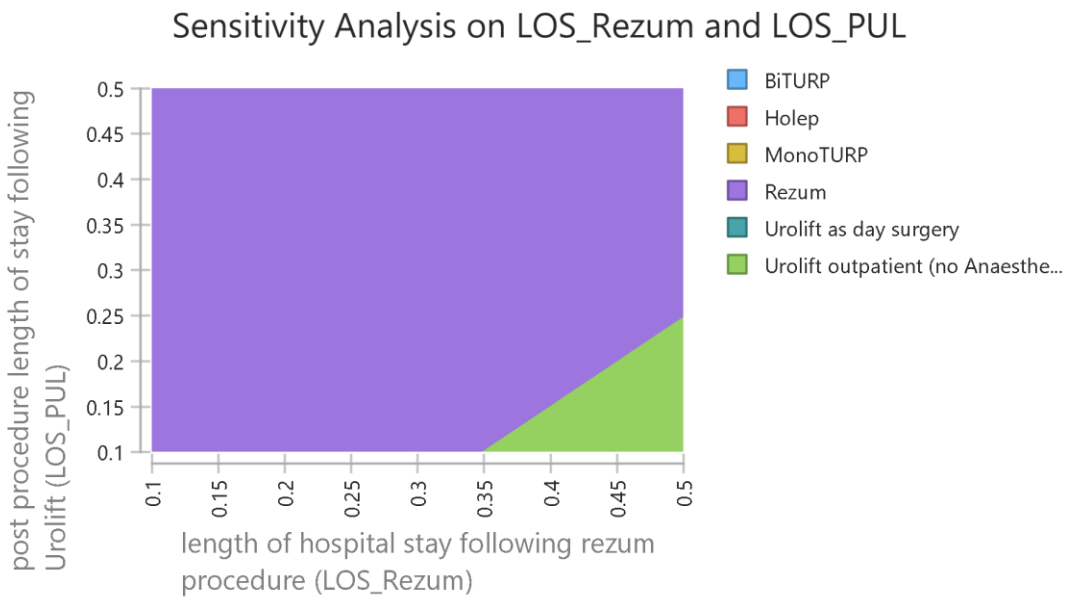

Figure 4 Two way sensitivity analysis for length of stay following Rezum and Urolift

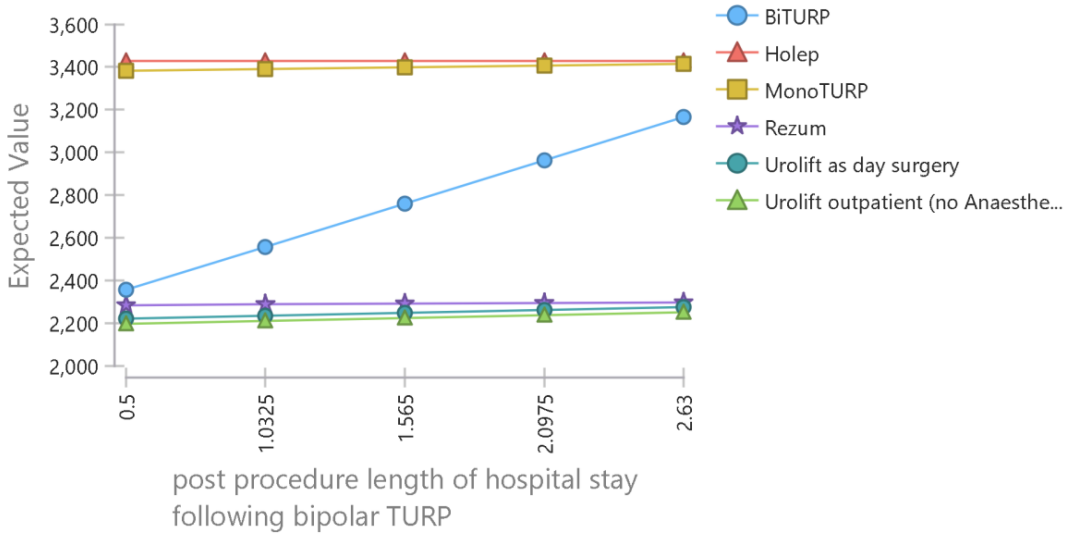

Figure 5 One way sensitivity analysis for length of hospital stay following bipolar TURP

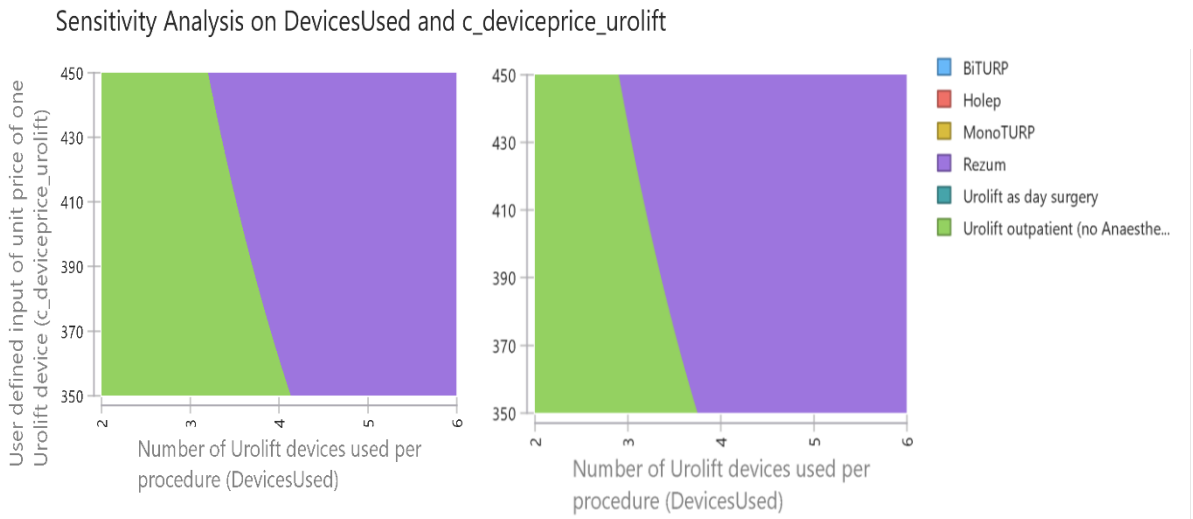

Figure 6Two way sensitivity analysis for number and price of Urolift devices

8.4 *The EAC's interpretation of the economic evidence*

The EAC have updated costs in the submitted model, resulting in a small reduction in cost savings for Urolift, with daycase surgery being approximately cost neutral compared to Rezum. This cost saving / cost neutral position is based on a reduction devices used and in theatre time for Urolift, both based on patient data submitted by the company.

In addition Urolift is only cost saving / neutral where the length of stay for Rezum is taken from MTG49 as 0.5 days, but with Urolift at 0.125 days. Both values have previously been accepted in published guidance documents, however MTG49 was based on the assumption that Urolift and Rezum both have the same length of stay. Where this is the case Urolift is no longer cost saving (at either 0.5 or 0.125 days stay).

The other contributory factor for Urolift's cost saving / cost neutral position is that Urolift has a telephone follow-up with a nurse, whereas other procedures have an outpatients appointment with a consultant.

To conclude, Urolift is cost saving compared to mono TURPS, biTURPS or HoLEP in the EAC base case and the scenarios explored. Urolift is also either cost saving or cost neutral compared to Rezum in the EAC base case, however this is dependent on several assumptions. The majority of the

scenarios exploring these assumptions result in Rezum becoming cost saving compared to either of the Urolift branches of the model.

9 Conclusions

9.1 *Conclusions from the clinical evidence*

The evidence base is of moderate to high quality with the main concern being the BPH6 study (Sonksen et al; 2015 and Gratzke et al; 2017) not being blinded to patient or outcome assessor. In addition this study did not state whether ITT analysis was performed which could have biased the results if not. In the non-comparative studies, 3 out of 5 studies had sample sizes <20 which limits the generalisability of the results. However, all outcomes, populations, interventions and comparators included were relevant to the scope. No evidence was included in relation to subgroups mentioned in the scope.

These results are mixed and suggested that whilst UroLift improves symptoms over time, this improvement is not as big as TURP for several symptom and urological outcome measures. When comparing to Rezum however, UroLift patients had bigger improvements for symptom severity and erectile dysfunction measures. When looking at outcomes over time UroLift does appear to improve patient's symptoms over a long timeframe. In addition, the number of adverse events were reduced in UroLift patients when compared to TURP.

The included NICE SLCS suggest that UroLift, when used in an NHS setting, is beneficial to patients and can be performed under local anaesthetic as a day case. To support this, the evidence base showed catheterisation rates, catheterisation time and hospitalisation times were reduced when using UroLift. This could prove beneficial to the NHS with potential cost savings.

There is a significant gap in the evidence as few of the included studies were conducted in an UK/NHS setting. This makes the results much less generalisable to this setting and so must be used with caution.

9.2 *Conclusions from the economic evidence*

The EAC have updated costs in the submitted model, resulting in a small reduction in cost savings for Urolift, The EAC base case shows Urolift (no anaesthetist) as slightly cost saving compared to all comparators, and Urolift (with anaesthetist) being approximately cost neutral compared to Rezum and cost saving compared to all other comparators. This cost saving / cost neutral position is based on a number of assumptions which do not all have a strong evidence base.

The following are key assumptions based on unpublished [redacted] provided by the company:

- Urolift theatre time is reduced from 30 minutes to 14 minutes
- Urolift devices used per procedure have reduced from 4 to 3.5

The following are key assumptions with no evidence base provided:

- Rezum has a longer length of stay (0.5 days) than Urolift (0.125 days)
- Urolift follow up is by telephone call with a nurse, whereas all other procedures require an outpatient visit with a consultant.

To conclude, Urolift is cost saving compared to mono TURPS, biTURPS or HoLEP in the EAC base case and the scenarios explored. Urolift is also either cost saving or cost neutral compared to Rezum in the EAC base case, however this is dependent on several assumptions. If any of the key assumptions for theatre time, number of devices or length of stay are not correct, this could result in Rezum becoming cost saving compared Urolift (either with or without anaesthetist).

10 Summary of the combined clinical and economic sections

The clinical evidence included, whilst of moderate to good quality, is lacking in number conducted within the UK. The comparative studies produced mixed results with some suggesting UroLift to be comparable to TURP or Rezum and some showing UroLift to be worse across different outcomes.

The economic evidence is strongly dependent on the submitted [redacted] for theatre time and number of devices used, plus an assumption of shorter length of stay for Urolift than other procedures, in particular Rezum. The base case is very slightly cost saving, compared to Rezum, where the company assumptions on these parameters is accepted. If the length of stay for Rezum and Urolift are similar, then Urolift is no longer cost saving compared to Rezum. Urolift remains cost saving in the model compared to the other technologies during one way sensitvitiy analysis and scenario modelling.

11 Implications for research

Both large clinical research and economic studies conducted in the UK are vital to know whether UroLift should be implemented within the NHS.

12 References

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13 Appendices

Use the appendices to describe additional data and information as needed – we've given some examples as a guide.

List the titles of the appendices here.

Appendix A – Search strategies
Appendix B – PRISMA diagram
Appendix C – Critical appraisals
Appendix D – Economic evidence
Appendix E – Stress test of submitted economic model

Appendix A – Search Strategies

Cochrane Library

ID	Search	Hits
#1	MeSH descriptor: [Lower Urinary Tract Symptoms] explode all trees	3174
#2	MeSH descriptor: [Prostatic Hyperplasia] this term only	1745
#3	MeSH descriptor: [Prostatism] explode all trees	65
#4	MeSH descriptor: [Urethral Obstruction] this term only	33
#5	MeSH descriptor: [Urinary Bladder Neck Obstruction] this term only	176
#6	(LUTS):ti,ab,kw (Word variations have been searched)	1221
#7	((urin* NEAR/3 tract* NEAR/3 (sympt* or block*))):ti,ab,kw (Word variations have been searched)	2636
#8	((urin* or urethra*) NEAR/3 (obstruct* or block*)):ti,ab,kw (Word variations have been searched)	778
#9	((Prostat* NEAR/3 Hyperplas*)):ti,ab,kw (Word variations have been searched)	3264
#10	((prostat* NEAR/3 hypertroph*)):ti,ab,kw (Word variations have been searched)	1674
#11	((prostat* NEAR/3 adenoma*)):ti,ab,kw (Word variations have been searched)	100
#12	(Prostatism):ti,ab,kw (Word variations have been searched)	20038
#13	(BPH):ti,ab,kw (Word variations have been searched)	2012
#14	{or #1-#13}	23948
#15	((uroLift or NeoTract)):ti,ab,kw (Word variations have been searched)	45
#16	MeSH descriptor: [Urologic Surgical Procedures, Male] this term only	108
#17	((Prostat* NEAR/3 lift*)):ti,ab,kw (Word variations have been searched)	69
#18	((urethra* NEAR/3 lift*)):ti,ab,kw (Word variations have been searched)	71
#19	{or #15-#18}	186

#20 #14 and #19 with Cochrane Library publication date Between Jan 2014 and Jul 2020, in Cochrane Reviews 2

#21 #14 and #19 with Publication Year from 2014 to 2020, in Trials 78

#22 #20 or #21 80

CRD (HTA and NHS EED)

1 MeSH DESCRIPTOR Lower Urinary Tract Symptoms EXPLODE ALL TREES IN NHSEED,HTA 190

2 (urolift or neotract) IN NHSEED, HTA 2

3 (urethra* and lift*) OR (prostat* and lift*) IN NHSEED, HTA 4

4 MeSH DESCRIPTOR Urologic Surgical Procedures, Male IN NHSEED,HTA 5

5 (LUTS or BPH or hyperplas*) IN NHSEED, HTA 174

6 #1 OR #5 358

7 #2 OR #3 OR #4 9

8 (#6 AND #7) IN NHSEED, HTA FROM 2014 TO 2020 2

Database: EMBASE <1947-Present>

1 prostate hypertrophy/ (38258)

2 urethra obstruction/ or urinary tract obstruction/ or bladder obstruction/ (12040)

3 Prostatitis/ (8937)

4 lower urinary tract symptom/ (14881)

5 LUTS.tw. (8539)

6 (urin* adj3 tract* adj3 (sympt* or block*)).tw. (16510)

7 ((urin* or urethra*) adj3 (obstruct* or block*)).tw. (10123)

8 (Prostat* adj3 Hyperplas*).tw. (23627)

9 (prostat* adj3 hypertroph*).tw. (4928)

10 (prostat* adj3 adenoma*).tw. (2288)

11 Prostatism.tw. (741)

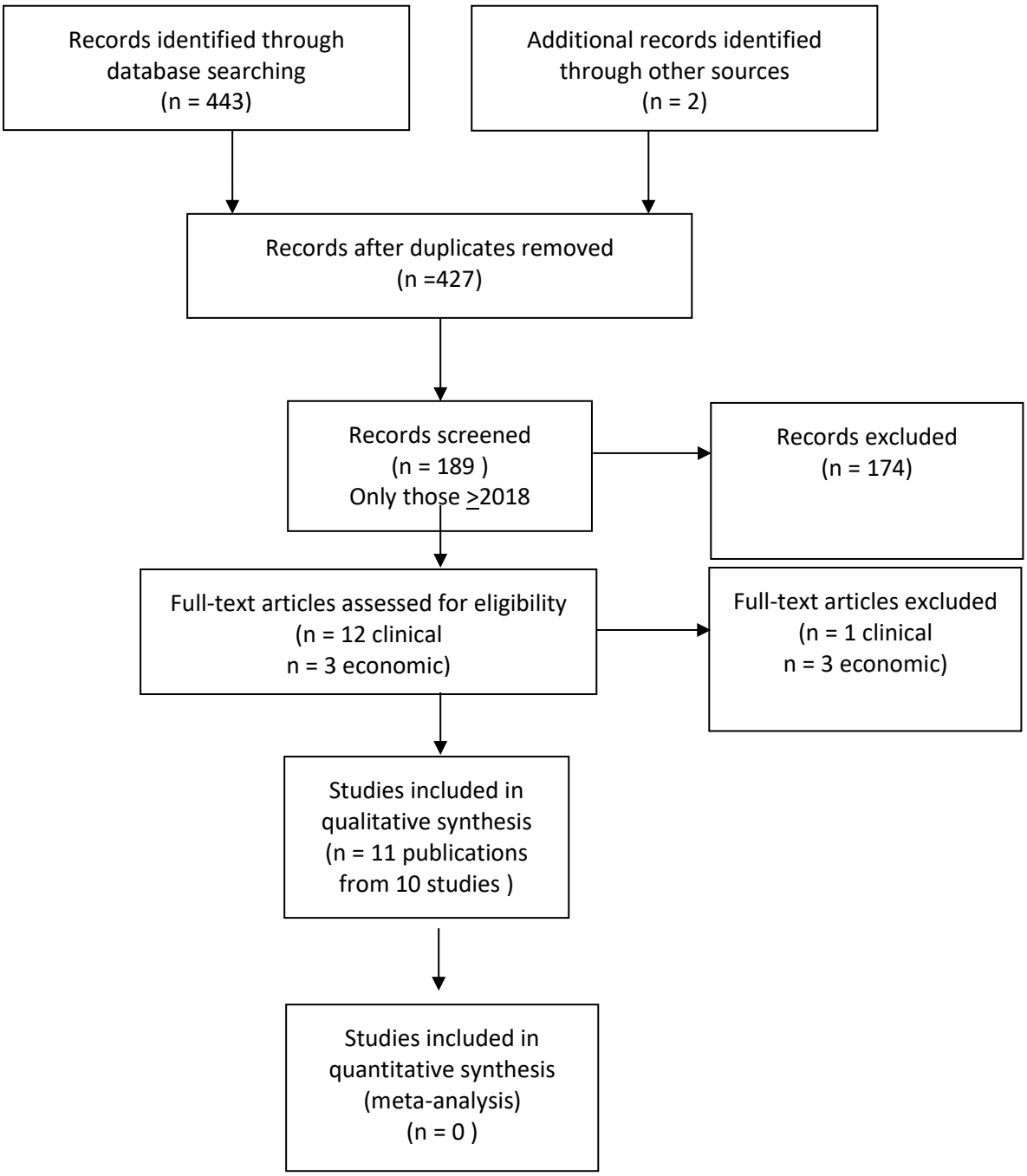
12 BPH.tw. (17446)
13 or/1-12 (83252)
14 (uroLift or NeoTract).tw. (177)
15 male genital system surgery/ (3008)
16 (urethra* adj3 lift*).tw. (257)
17 (Prostat* adj3 lift*).tw. (245)
18 14 or 15 or 16 or 17 (3333)
19 13 and 18 (382)
20 limit 19 to yr="2014 -Current" (281)

Database: Ovid MEDLINE(R) ALL <1946 to July 10, 2020>

1 exp Lower Urinary Tract Symptoms/ (40410)
2 Prostatic Hyperplasia/ (21833)
3 Prostatitis/ (5494)
4 urethral obstruction/ or urinary bladder neck obstruction/ (6354)
5 LUTS.tw. (4233)
6 (urin* adj3 tract* adj3 (sympt* or block*)).tw. (10246)
7 ((urin* or urethra*) adj3 (obstruct* or block*)).tw. (6642)
8 (Prostat* adj3 Hyperplas*).tw. (16682)
9 (prostat* adj3 hypertroph*).tw. (3368)
10 (prostat* adj3 adenoma*).tw. (1484)
11 Prostatism.tw. (595)
12 BPH.tw. (11454)
13 or/1-12 (85967)
14 (uroLift or NeoTract).tw. (70)
15 urologic surgical procedures, male/ (3502)
16 (urethra* adj3 lift*).tw. (107)
17 (Prostat* adj3 lift*).tw. (100)
18 14 or 15 or 16 or 17 (3627)
19 13 and 18 (480)
20 exp animals/ not humans.sh. (4715987)
21 19 not 20 (471)

22 limit 21 to yr="2014 -Current" (247)

Appendix B - PRISMA Flow Diagram



Appendix C - Quality appraisals

Quality assessment of included randomised controlled trials assessed by the Cochrane Risk of Bias tool (Sterne et al. 2019)

Risk of Bias Domain	Roehrborn et al (2015 and 2017) 0 L.I.F.T study
Bias arising from the randomization process	Low
Bias due to deviations from intended interventions	Low
Bias due to missing outcome data	Low
Bias in measurement of the outcome	Low
Bias in selection of the reported result	Low
Overall risk of bias	**Low**

Risk of Bias Domain	Sonksen et al (2015) and Gratzke et al (2017) – BPH6 study
Bias arising from the randomization process	Some concerns
Bias due to deviations from intended interventions	High
Bias due to missing outcome data	Some concerns
Bias in measurement of the outcome	Low
Bias in selection of the reported result	Low
Overall risk of bias	Some concerns

Quality assessment of included non-randomised comparative study assessed by the Joanna Briggs Institute Checklist for Quasi-Experimental Studies

Rukstalis et al (2016)	Yes	No	Unclear	N/A
Is it clear in the study what is the 'cause' and what is the 'effect'(i.e. there is no confusion about which variable comes first)?	✓			

Were the participants included in any comparisons similar?				✓ Crossover study
Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	✓			
Was there a control group?				✓ Crossover study
Were there multiple measurements of the outcome both pre and post the intervention/exposure?	✓			
Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?	✓			
Were the outcomes of participants included in any comparisons measured in the same way?				✓ Crossover study
Were outcomes measured in a reliable way?	✓			
Was appropriate statistical analysis used?	✓			
Comments	Was a crossover study comparing outlook of those having undergone a subsequent procedure. Patients acted as their own 'controls'.			
Rukstalis et al (2018)	**Yes**	**No**	**Unclear**	**N/A**
Is it clear in the study what is the 'cause' and what is the 'effect'(i.e. there is no confusion about which variable comes first)?	✓			
Were the participants included in any comparisons similar?	✓			
Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	✓			

Was there a control group?	✓			
Were there multiple measurements of the outcome both pre and post the intervention/exposure?	✓			
Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?	✓			
Were the outcomes of participants included in any comparisons measured in the same way?	✓			
Were outcomes measured in a reliable way?	✓			
Was appropriate statistical analysis used?				✓
Comments	Results are slightly unclear as to which participants are actually part of the comparison group.			

Tutrone and Schiff (2020)	**Yes**	**No**	**Unclear**	**N/A**
Is it clear in the study what is the 'cause' and what is the 'effect'(i.e. there is no confusion about which variable comes first)?	✓			
Were the participants included in any comparisons similar?	✓			
Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	✓			
Was there a control group?	✓			
Were there multiple measurements of the outcome both pre and post the intervention/exposure?	✓			

Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?	✓			
Were the outcomes of participants included in any comparisons measured in the same way?	✓			
Were outcomes measured in a reliable way?	✓			
Was appropriate statistical analysis used?	✓			
Comments	Other than non-randomised no significant issues identified, baseline characteristics were similar.			

Quality assessment of the included non-comparative studies using the NIH National Heart, Lung and Blood Institute Before and After tool

Bozkurt et al (2016)

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the study question or objective clearly stated?	✓		
2. Were eligibility/selection criteria for the study population prespecified and clearly described?	✓		
3. Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?	✓		
4. Were all eligible participants that met the prespecified entry criteria enrolled?	✓		
5. Was the sample size sufficiently large to provide confidence in the findings?		✓	
6. Was the test/service/intervention clearly described and delivered consistently across the study population?	✓		
7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?	✓		
8. Were the people assessing the outcomes blinded to the participants' exposures/interventions?			✓
9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?	✓		

Criteria	Yes	No	Other (CD, NR, NA)*
10. Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?	✓		
11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)?	✓		
12. If the intervention was conducted at a group level (e.g., a whole hospital, a community, etc.) did the statistical analysis take into account the use of individual-level data to determine effects at the group level?			✓

Quality Rating = Good

Bardoli et al (2017)

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the study question or objective clearly stated?	✓		
2. Were eligibility/selection criteria for the study population prespecified and clearly described?	✓		
3. Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?	✓		
4. Were all eligible participants that met the prespecified entry criteria enrolled?	✓		
5. Was the sample size sufficiently large to provide confidence in the findings?		✓	
6. Was the test/service/intervention clearly described and delivered consistently across the study population?	✓		
7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?		✓	
8. Were the people assessing the outcomes blinded to the participants' exposures/interventions?			✓
9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?	✓		
10. Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?	✓		
11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)?		✓	
12. If the intervention was conducted at a group level (e.g., a whole hospital, a community, etc.) did the statistical analysis take into account the use of individual-level data to determine effects at the group level?			✓

Quality Rating = Fair

Eure et al (2019)

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the study question or objective clearly stated?	✓		
2. Were eligibility/selection criteria for the study population prespecified and clearly described?		✓	
3. Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?	✓		
4. Were all eligible participants that met the prespecified entry criteria enrolled?		✓	
5. Was the sample size sufficiently large to provide confidence in the findings?	✓		
6. Was the test/service/intervention clearly described and delivered consistently across the study population?	✓		
7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?	✓		
8. Were the people assessing the outcomes blinded to the participants' exposures/interventions?			✓
9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?		✓	
10. Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?	✓		
11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)?	✓		
12. If the intervention was conducted at a group level (e.g., a whole hospital, a community, etc.) did the statistical analysis take into account the use of individual-level data to determine effects at the group level?			✓

Quality Rating = Fair

Rubio et al (2019)

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the study question or objective clearly stated?	✓		
2. Were eligibility/selection criteria for the study population prespecified and clearly described?	✓		
3. Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?	✓		
4. Were all eligible participants that met the prespecified entry criteria enrolled?	✓		
5. Was the sample size sufficiently large to provide confidence in the findings?		✓	
6. Was the test/service/intervention clearly described and delivered consistently across the study population?	✓		
7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?	✓		
8. Were the people assessing the outcomes blinded to the participants' exposures/interventions?			✓
9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?	✓		
10. Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?	✓		
11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)?	✓		
12. If the intervention was conducted at a group level (e.g., a whole hospital, a community, etc.) did the statistical analysis take into account the use of individual-level data to determine effects at the group level?			✓

Quality Rating = Good

Sievert et al (2019)

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the study question or objective clearly stated?	✓		
2. Were eligibility/selection criteria for the study population prespecified and clearly described?		✓	
3. Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?	✓		
4. Were all eligible participants that met the prespecified entry criteria enrolled?		✓	
5. Was the sample size sufficiently large to provide confidence in the findings?	✓		
6. Was the test/service/intervention clearly described and delivered consistently across the study population?	✓		
7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?	✓		
8. Were the people assessing the outcomes blinded to the participants' exposures/interventions?			✓
9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?		✓	
10. Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?	✓		
11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)?	✓		
12. If the intervention was conducted at a group level (e.g., a whole hospital, a community, etc.) did the statistical analysis take into account the use of individual-level data to determine effects at the group level?			✓

Quality Rating = Fair

Appendix D – Economic evidence results

<table>
<tr><th>Country, study type and intervention details</th><th>Study population, design and data sources</th><th>Costs: description and values</th><th>Outcomes: description and values</th><th>Results: Cost effectiveness</th><th>Notes</th></tr>
<tr>
<td>Ulchaker & Martinson 2018

Country: US

Study Type:
Cost Effectiveness

Interventions and Management:
Multiple interventions:
• Medication
• Rezum
• UroLift
• Prostiva
• Greenlight PVP
• TURP</td>
<td>Study Population:
Design: Markov Model
Payers perspective
2 year time horizon
6 month cycle
Data Sources:
Sources of effectiveness data:
Literature search 2001-17
Sources of resource use data:
Literature search 2001-17
Utility
IPSS score
Sources of unit cost data:
2016 Medicare fee schedules

Sensitivity Analysis:
Probabilistic, no one way</td>
<td>Full costs not extracted as not relevant to UK healthcare system

Costs included for Treatment, retreatment and adverse events

First retreatment for medication or MIT methods is MIT (equal split between Resum, Urloft and Postivia)
Second retreatment is PVP or TURP</td>
<td>Outcomes: Presented for Rezum, Urolift and TURPS only
Utility & Treatment effectiveness
<table>
<tr><td></td><td colspan="2">Utility
Change in IPSS</td><td>Effectiveness
Return of LUTS</td></tr>
<tr><td></td><td>Yr1</td><td>Yr2</td><td>% patients per cycle</td></tr>
<tr><td>Rezum</td><td>-11.65</td><td>-11.80</td><td>0.60</td></tr>
<tr><td>Urolift</td><td>-10.65</td><td>-9.47</td><td>4.92</td></tr>
<tr><td>TURPS</td><td>-16.79</td><td>-13.06</td><td>0.31</td></tr>
</table>
Adverse Events
<table>
<tr><td></td><td colspan="2">Incontinence</td><td colspan="2">Stricture . contracture / stenosis</td></tr>
<tr><td></td><td>Early</td><td>Late</td><td>Early</td><td>Late</td></tr>
<tr><td>Rezum</td><td>0.01</td><td>0.01</td><td>1.13</td><td>0.42</td></tr>
<tr><td>Urolift</td><td>1.05</td><td>0.97</td><td>0.01</td><td>0.01</td></tr>
<tr><td>TURPS</td><td>2.06</td><td>0.78</td><td>4.66</td><td>0.62</td></tr>
</table>
<table>
<tr><td></td><td>AUR</td><td>ED</td><td colspan="2">UTI</td></tr>
<tr><td></td><td>Yr2</td><td>Early</td><td>Early</td><td>Late</td></tr>
<tr><td>Rezum</td><td>0.27</td><td>0.01</td><td>1.99</td><td>0.43</td></tr>
<tr><td>Urolift</td><td>1.31</td><td>0.01</td><td>2.17</td><td>0.64</td></tr>
<tr><td>TURPS</td><td>1.76</td><td>1.05</td><td>12.23</td><td>2.09</td></tr>
</table>
</td>
<td>Base Case
<table>
<tr><td></td><td>Rezum</td><td>Urolift</td><td>TURPS</td></tr>
<tr><td>Cost</td><td>$2,582</td><td>$6,386</td><td>$5,181</td></tr>
<tr><td>IPss</td><td>10.2</td><td>11.4</td><td>6.4</td></tr>
<tr><td>CE of Rezum</td><td>-</td><td>-$352</td><td>$686</td></tr>
<tr><td>CE of TURPS</td><td>$6,863</td><td>-$240</td><td>-</td></tr>
</table>
Probabilistic sensitivity analysis
Urolift was less effective and more costly than Rezum in all scenarios</td>
<td>Conclusions:
Urolift is dominated by Rezum and TURPS

Limitations:

US payer perspective. Not directly relevant to UK</td>
</tr>
</table>

<table>
<tr><th>Country, study type and intervention details</th><th>Study population, design and data sources</th><th>Costs: description and values</th><th>Outcomes: description and values</th><th>Results: Cost effectiveness</th><th>Notes</th></tr>
<tr>
<td>DeWitt-Foy et al. 2019
Country: US

Study Type:
Cost equivalence

Interventions and Management:
Inpatient surgery:
Robotic, open
Outpatient surgery:
Button vaporization
Robotic, PVP, TURP
Office based
Convective water vapor ablation
Urethral lift
Medication</td>
<td>Study Population:
Design: Simple costing
Payer perspective

Data Sources:
Sources of effectiveness data:
Not modelled

Sources of resource use data:
N/A

Utility: Not modelled

Sources of unit cost data: 2018 Medicare reimbursement data

Sensitivity Analysis: None</td>
<td>Simple collection of reimbursement cost for each procedure.
No modelling
Time equivalence calculated using Medication as a baseline, with 1 year.</td>
<td>Outcomes:

Utility: Not modelled
Treatment effectiveness:
Not modelled

Adverse Events: Not modelled</td>
<td>Base Case
<table>
<tr><th></th><th></th><th>Treatment cost</th></tr>
<tr><td>Inpatient</td><td>Robotic</td><td>$11,583</td></tr>
<tr><td></td><td>Open</td><td>$7,088</td></tr>
<tr><td>Outpatient</td><td>Button</td><td>$3,643</td></tr>
<tr><td></td><td>Robotic</td><td>$6,777</td></tr>
<tr><td></td><td>PVP</td><td>$3,719</td></tr>
<tr><td></td><td>TURPS</td><td>$3,295</td></tr>
<tr><td>Office</td><td>CWVA</td><td>$830</td></tr>
<tr><td></td><td>PUL</td><td>$3,779</td></tr>
<tr><td>Meds</td><td>Meds</td><td>$1,435</td></tr>
</table>
Summary
<table>
<tr><th></th><th colspan="2">DeWitt-Foy 2019</th><th colspan="2">Gill 2018</th><th colspan="2">Ulchaker 2017</th></tr>
<tr><th></th><th>cost</th><th>yrs</th><th>cost</th><th>yrs</th><th>cost</th><th>yrs</th></tr>
<tr><td>TURPS</td><td>$3,295</td><td>2.30</td><td>$1,667</td><td>1.01</td><td>$5,181</td><td>2.98</td></tr>
<tr><td>CWVA</td><td>$830</td><td>0.58</td><td>$1,742</td><td>1.05</td><td>$2,582</td><td>1.49</td></tr>
<tr><td>PUL</td><td>$3,779</td><td>2.63</td><td>$2,721</td><td>1.64</td><td>$6,386</td><td>3.68</td></tr>
</table>
Probabilistic sensitivity analysis
N/A</td>
<td>Conclusions:
PUL is a more expensive procedure than TURPS or CWVA

Limitations:

No modelling, no consideration of effectiveness, no inclusion of repeat treatments or adverse events.
US study.</td>
</tr>
</table>

Appendix E – Stress testing submitted update model

Scenario	Urolift out	Urolift day	Rezum	Bi Turp	Mono Turp	HOLEP	Notes
Base case	£2,240	£2,265	£2,306	£3,297	£3,388	£3,543	Submitted update model (TreeAge)
Urolift fail = 0%	£1,748	£1,773	£2,306	£3,297	£3.388	£3,543	No second procedures for Urolift, all others unchanged
Urolift fail = 100%	£5,379	£5,395	£2,306	£3,297	£3.388	£3,543	All Urolift require a second procedure, costs increase, others unchanged
Rezum fail = 0%	£2,240	£2,265	£2,165	£3,297	£3,388	£3,543	No second procedures for Rezum, all others unchanged
Rezum fail = 100%	£2,240	£2,265	£5,327	£3,297	£3,388	£3,543	All Rezum require a second procedure, costs increase, others unchanged
Cost of urolift = £1	£760	£784	£2,306	£3,297	£3,388	£3,543	Low cost of Urolift, as expected, others unchanged, no other procedures use Urolift as second option, but approx. 1/3 of Urolift fails use Urolift as second option, so additional cost savings for Urolift
Cost of Urolift = £1000	£4,467	£4,491	£2,306	£3,297	£3,388	£3,543	High cost of Urolift, as expected, others unchanged, no procedures use Urolift as second option, but approx. 1/3 of Urolift fails use Urolift as second option, so additional increase.
Time horizon = 6 months	£1,796	£1,822	£2,298	£2,961	£3,052	£3,221	Reduced cost of incontinence products over time plus variation in Urolift failure rate at different time horizonz.
Time horizon = 20 years	£2,339	£2,363	£2,329	£4,417	£4,508	£4,613	Rezum becomes most cost saving option – less second procedues are TURP and therefore less incontinence.
Pincontinence=0	£2,308	£2,232	£2,298	£2,928	£3,019	£3,189	

Time horizon = 6 months	£1,796	£1,821	£2,298	£2,928	£3,019	£3,189	Urolift is a lot cheaper, but Rezum is almost unchanged. This is because Urolift has more failures, and more of these are TURP therfore more likely to get incontinence patients. Rezum has few failures and 50% of repeats are with Rezum -all of which have 0% probability of incontinence. In addition Urolift failure rates are set for different time points.
Time horizon = 20 years	£2,208	£2,312	£2,298	£2,928	£3,019	£3,189	As above, in reverse.
Cost incontinence = 0, time =0.5 years	£1,796	£1,821	£2,298	£2,928	£3,019	£3,189	In addition to incontinence products, the other factor that changes over time is the likelihood of failure. This is only the case for Urolift in practice.
Cost incontinence = 0, time =20 years	£2,208	£2,312	£2,298	£2,928	£3,019	£3,189	Incontinence costs will accumulate over 20 years, but likelihood of failure is only given rates up to 5 years, and so this rate will be used at any time point beyond 5 years.

Appendix F – Scenario results

Variable	Out	Day	Rezum	BiTURP	MTURP	HoLEP
Company base case	**2240.414**	**2264.62**	**2305.564**	**3296.903**	**3387.827**	**3542.552**
	24.206	*0*	*-40.9441*	*-1032.28*	*-1123.21*	*-1277.93*
EAC base case	**2250.466**	**2274.672**	**2297.419**	**3165.618**	**3414.869**	**3428.002**
	24.206	*0*	*-22.7474*	*-890.947*	*-1140.2*	*-1153.33*
LOS Resum = 0.125	2250.466	2274.672	2157.503	3165.618	3414.869	3428.002
	24.206	*0*	*117.169*	*-890.947*	*-1140.2*	*-1153.33*
LOS Rezum and Urolift = 0.5	2393.207	2417.413	2297.419	3165.618	3414.869	3428.002
	24.206	*0*	*119.994*	*-748.205*	*-997.456*	*-1010.59*
Follow up costs= £37.67 for all comparators	2237.033	2261.239	2221.875	3089.22	3338.47	3355.672
	24.206	*0*	*39.3646*	*-827.98*	*-1077.23*	*-1094.43*
LOS BiTURP = 0.5	2196.322	2220.528	2284.462	2355.367	3382.067	3428.002
	24.206	*0*	*-63.9337*	*-134.839*	*-1161.54*	*-1207.47*
All theatre staff costs set at zero (double counting)	2141.234	2141.234	2186.169	2839.557	3033.596	2985.023
	0	*0*	*-44.9348*	*-698.324*	*-892.362*	*-843.79*
c_UTI = £935.60	2250.873	2275.079	2301.654	3166.865	3416.115	3439.621
	24.206	*0*	*-26.5749*	*-891.786*	*-1141.04*	*-1164.54*
1% incontinence for Rezum and Urolift	2356.669	2380.888	2404.818	3165.618	3414.869	3428.002
	24.2187	*0*	*-23.9302*	*-784.731*	*-1033.98*	*-1047.11*
Theatre time Urolift = 30	2528.93	2580.8	2297.419	3165.618	3414.869	3428.002
	51.87	*0*	*283.381*	*-584.819*	*-834.069*	*-847.202*

MT241 Urolift Update

Request for additional work post MTAC

Following MTAC, errors in the submitted model were noted and have been corrected. In addition the EAC have been requested to make changes to the follow-up consultation methods, trial without catheter location and use of cystoscopy. The EAC have also been requested to present the model results separately for treatment with and without the presence of an obstructive median lobe.

1 Correction of errors identified in the model

1.1 Ensure that correct variables used for 1st and 2nd procedure

Errors in the submitted model were noted by the EAC, after MTAC. These included an error where the cost calculations after a second procedure were not retaining the correct values for some of the variables initially defined in the first procedure. The EAC have corrected this in the model. The total impact was small, with no change in the rankings of the technologies, and a slight increase in the cost saving of Urolift compared to the alternatives.

1.2 UTI rate for Urolift

For MTG26, the company used a rate of 1.4%, stating that this was based on Roehrborn 2013. However the paper reports a rate of 2.9% for the first 3 months after the procedure. This was unchallenged for MTG26, but MTG49 used the correct rate of 2.9%

The current submission uses 5 year data from the same LIFT study (Roehrborn 2017), and gives a value of 0.1% is for the first 3 months. The reason is that 0.1% is the percentage of subject months with UTI in months 0-3, rather than the % of patients that had UTI at any point in 0-3 months. I missed this distinction when reviewing.

Following both changes, the corrected EAC base case is:

	EAC base case at MTAC meeting		**Corrected EAC base case**	
	Per patient cost	Incremental cost vs. Urolift	Per patient cost	Incremental cost vs. Urolift
Urolift - outpatient	£2,250		£2,160	
Urolift – day case	£2,275	£24	£2,185	£25
Rezum	£2,297	£47	£2,281	£121
Bi TURP	£3,166	£915	£3,166	£1,006
MonoTURP	£3,415	£1,164	£3,427	£1,267
HOLEP	£3,428	£1,178	£3,415	£1,255

2 Change to visit costs

2.1 All follow-up visits by telephone consultation

Urolift follow up visits were costed at £37.67, for a 20 minute telephone consultation with a nurse in the EAC base case presented to the committee. All other technologies had a follow-up with a consultant at a cost of £110 for an outpatient appointment. .

Following the MTAC meeting, the EAC have changed all follow up visits to be by telephone, at a cost of £37.60. Urolift remained cost saving following this change.

2.2 TWOC appointment in community

The EAC base case used a cost of £135 for an outpatient procedure (HRG LB15E. National Reference cost (2018/19)), based on an update of the submitted model. Following the MTAC request, the EAC have updated this to reflect a community appointment, using NHS Reference cost (2018/19) N14AF Specialist Nursing Continence Services, Adult face to face £83. This resulted in a slightly lower cost for Rezum, which then becomes cost saving compared to Urolift:

2.3 Flexible cystoscopy for all Urolift patients

The need for this for Urolift was brought up in the MTG26 committee meeting, and the EAC produced an additional piece of work stating that in additional consultations with experts there was consensus that the cost was similar for each procedure and so does not need to be included. Other pre-op tests were included, but were the same cost for each technique and so had no impact on the incremental cost.

A cost for flexible cystoscopy was added for all Urolift patients, however it should be noted that some experts did not routinely use flexible cystoscopy for all patients. The cost used was £187 (LB72A, Diagnostic Flexible Cystoscopy, 19 years and over, Outpatients, NHS Reference costs 2018/19)/

	Telephone visits		+TWOC in community		+ Flexible Cystoscopy	
	Per patient cost	Incremental cost vs. Urolift	Per patient cost	Incremental cost vs. Urolift	Per patient cost	Incremental cost vs. Urolift
Urolift - outpatient	£2,154		£2,154		£2,349	
Urolift – day case	£2,178	£24	£2,178	£24	£2,373	£24
Rezum	£2,206	£52	£2,153	-£1	£2,153	-£196
Bi TURP	£3,090	£936	£3,090	£936	£3,090	£741
MonoTURP	£3,351	£1,197	£3,351	£1,197	£3,351	£1,002
HOLEP	£3,343	£1,189	£3,343	£1,189	£3,343	£994

The results show the impact of each subsequent (and cumulative) change to the model.

3 Results presented separately for treatment with or without obstructive median lobe

This is achieved by setting the probability of having Obstructive Median Lobe (OML) to either 0 or 1. In addition the additional number of implants for OML was changed from 1.3 to 2. The only difference modelled is the number of implants. There are no differences in the procedure or outcomes in the model.

The results shown incorporate all the previous changes (corrections and updates to visit parameters).

	No OML, implants = 3.5		All OML, implants = 5.5	
	Per patient cost	Incremental cost vs. Urolift	Per patient cost	Incremental cost vs. Urolift
Urolift - outpatient	£2,321		£3,121	
Urolift – day case	£2,345	£24	£3,145	£24
Rezum	£2,153	-£168	£2,153	-£968
BiTURP	£3,090	£769	£3,090	-£31
MonoTURP	£3,351	£1,030	£3,351	£230
HOLEP	£3,343	£1,022	£3,343	£222

For procedures without treatment for OML, and incorporating all previous changes, Urolift is still not cost saving compared to Rezum. Where all treatment is for OML, and incorporating all previous changes, Urolift is not cost saving compared to Rezum or BiTURP.

This is result is dependent on all patients requiring flexible cystoscopy, which was not the practice of all the experts at the committee meeting. Where flexible cystoscopy is not included, Urolift would be very slightly cost saving compared to Rezum for no OML treatment, and would remain cost incurring compared to Rezum where all treatment was for OML.

4 Additional sensitivity analysis

The EAC have been requested to consider alternative values for the number of implants used, following discussion at MTAC. The number of implants used is a key driver for the model results, and varies between patients. For the purposes of economic modelling, the number of implants used should be the mean, which may be different from the median, or “typical patient”.

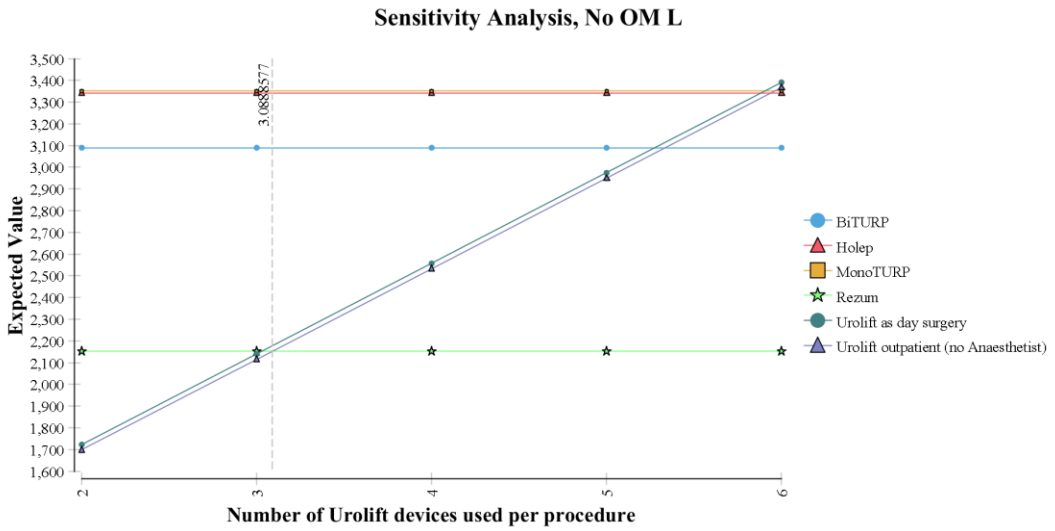


Figure 1 Sensitivity analysis with no OML

For the OML option (figure 2), the model assumes that all patients have OML at the first procedure, but it does not model any OML treatment for re-treatment. The sensitivity graph x-axis shows the base number of implants used, for any treatment. Where OML is present (in this scenario for all patients at first treatment), 2 extra implants are used, in addition to the number in figure2.

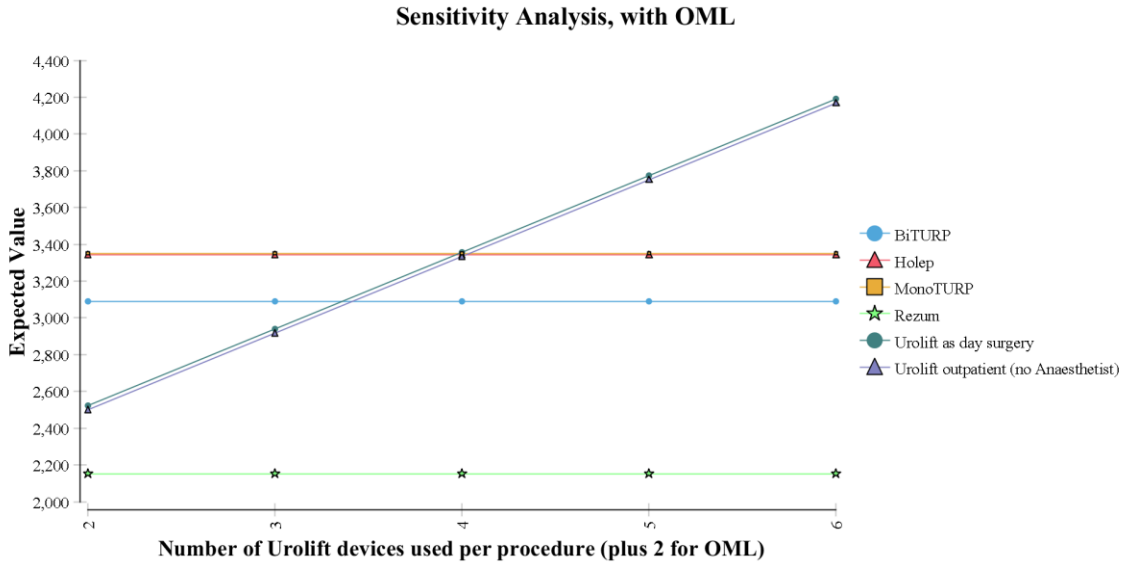


Figure 2 Threshold diagram with all patients assumed to have OML for first procedure

For a scenario where a mean of 4 implants are used the results for Urolift would be:

	No OML, implants = 4	All OML, implants = 6
	Per patient cost	Per patient cost
Urolift - outpatient	£2,533	£3,333
Urolift – day case	£2,557	£3,357

The results for other technologies would be unchanged.

5 Detailed description of changes to model

The following variables were redefined:

C_visit changed to c_visit1 and c_visit2

c_complications to c_compliactions1 and c_complications2

theatretime to theatretime1 and theatretime2

c_procedure to c_procedure1 and c_procedure2

pTWOC to pTWOC1 and pTWOC2

Variables for each of the complications were also redefined as 1 and 2.

For each of the second procedures, the variable_1 was deleted and replaced by the variable_2, thus avoiding the same variable name being given two values in one branch of the model.

In addition, errors were corrected for both Rezum (pRetention), Mono and BiTurp (pTransfusion) where an incorrect distribution had been referenced for the complication. These had minimal impacts on the model.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology guidance

Assessment report update overview

MT241 UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia

(update of MTG26 UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia)

This assessment report update overview has been prepared by the Medical Technologies Evaluation Programme team to highlight the significant findings of the External Assessment Centre (EAC) report. It includes **brief** descriptions of the key features of the evidence base and the cost analysis, any additional analysis carried out, and additional information, uncertainties and key issues the Committee may wish to discuss. It should be read along with the company submission of evidence and with the EAC assessment report update. The overview forms part of the information received by the Medical Technologies Advisory Committee when it develops its recommendations on the technology.

Key issues for consideration by the Committee are described in section 6, following the brief summaries of the clinical and cost evidence.

This report contains information that has been supplied in confidence and will be redacted before publication. This information is highlighted in [redacted]. This overview also contains:

- Appendix A: Sources of evidence
- Appendix B: Comments from professional bodies

- Appendix C: Comments from patient organisations

1 The technology

The UroLift system (NeoTract) is used to perform a prostatic urethral lift, a procedure that is an alternative to current standard surgical interventions such as transurethral resection of the prostate (TURP) and holmium laser enucleation (HoLEP). The UroLift system uses adjustable, permanent implants to pull excess prostatic tissue away so that it does not narrow or block the urethra. In this way, the device is designed to relieve symptoms of urinary outflow obstruction without cutting or removing tissue. The procedure can be done with the patient under local or general anaesthetic and may be done either on an in-patient or day-case basis. The UroLift system received a CE mark in November 2009 as a prostatic retraction implant for use in treating urinary outflow obstruction secondary to benign prostatic hyperplasia. The instructions for use specify that it is indicated for use in men aged 50 years and older and is contraindicated in men that have prostates larger than 100 ml.

2 Proposed use of the technology

2.1 Disease or condition

Urolift is intended for use for the treatment of symptoms due to urinary outflow obstruction secondary to benign prostatic hyperplasia (BPH). BPH is the most common cause of lower urinary tract symptoms, which include poor urinary stream, frequent urination and nocturia (the need to wake and urinate at night). If untreated, BPH can result in urinary tract infection, acute or chronic urinary retention and kidney failure. Lower urinary tract symptoms secondary to BPH do not usually cause severe illness, but they may affect normal daily activities and sexual function, and may indicate more serious urogenital problems.

2.2 Patient group

Urolift is intended for use for the treatment of symptoms due to urinary outflow obstruction secondary to benign prostatic hyperplasia (BPH), including lateral and median lobe hyperplasia [indication added for 2020 guidance update], in men 45 years of age or older. It should not be used for men who have a prostate volume of more than 100 ml, or those who have a urinary tract infection, urethral conditions that prevent the insertion of the delivery system into the bladder, urinary incontinence due to incompetent sphincter, or current gross haematuria.

The prevalence of BPH increases with age; around 60% of men aged 60 or older and over 80% of men aged 70 or older experience some symptoms due to BPH. The first pathological signs of BPH are seen in men aged 31-40, although prevalence is typically only 8%. This rate increases rapidly with age: around 60% of men aged 60 or older will experience some degree of prostate enlargement (NHS Choices), and over 80% of men aged 70 or older (Woo, 2012). BPH is the most common cause of lower urinary tract symptoms (LUTS), although the two are not necessarily synonymous. Moderate-to-severe LUTS are present in about 40% of men older than 50 years of age, rising to 90% of men in their eighties (Patient UK). Moderate to severe LUTS are estimated to affect up to 3.4 million men in the UK (Rees, 2014), and up to 15,000 men undergo TURP annually in England and Wales to relieve symptoms (NHS Direct Wales).

2.3 Current management

NICE CG97 Lower urinary tract symptoms in men: management (2010) recommended surgical interventions for men with BPH only when LUTS are severe or drug treatment and conservative management have been unsuccessful or are not appropriate. If symptoms worsen over time, or if conservative management or drug treatment options are inappropriate or unsuccessful, surgical options may be considered. For voiding LUTS, options include monopolar or bipolar TURP, transurethral vaporisation of the prostate (TUVP) or holmium laser enucleation of the prostate (HoLEP). Transurethral

incision of the prostate (TUIP) may be offered if the prostate is estimated to be smaller than 30 g. Open prostatectomy should only be offered if the prostate is estimated to be larger than 80 g. These treatments may be unsuitable for some people, due to the size and width of the prostate, size of the median lobe or position of the bladder neck. If the prostate is too large for transurethral surgical interventions, an open prostatectomy may be offered. All surgical comparators (except TUIP) functionally reduce prostate tissue volume by destroying tissue and debulking the prostate, to relieve LUTS.

Minimally invasive treatments such as transurethral needle ablation (TUNA), transurethral microwave thermotherapy (TUMT), high-intensity focused ultrasound (HIFU), transurethral ethanol ablation of the prostate (TEAP) and laser coagulation are not recommended by NICE for people with lower urinary tract obstructive symptoms (NICE guideline lower urinary tract symptoms in men: management). The clinical guideline recommends offering adjustable prostatic implants (such as the UroLift system) for the treatment of storage symptoms only as part of a randomised controlled trial. Insertion of prostatic urethral lift implants to treat lower urinary tract symptoms secondary to benign prostatic hyperplasia (NICE interventional procedure guidance 475) concluded that there is adequate evidence on the safety and efficacy of the procedure to support its use, provided that clinicians have specific training in the insertion of the implants.

2.4 Proposed management with new technology

Based on the company's proposed case for adoption, the Medical Technologies Evaluation Programme is considering the UroLift as an alternative option to TURP, HoLEP and Rezum. It would be used at the same point in the care pathway as these technologies, most likely after pharmaceutical treatment has failed or is no longer appropriate. Using the UroLift system does not preclude the subsequent use of other surgical procedures, such as TURP. A prostatic urethral lift can be done as a day surgery, and it is proposed that using the UroLift system would lead to fewer inpatient stays than TURP or HoLEP (which both require at least 1 overnight

stay). In this way, the UroLift may allow for patient care to be better structured around day surgeries and subsequent outpatient care. There would be a potential reduction in complications associated with inpatient BPH procedures, such as nosocomial infection, urinary tract infections related to post-operative catheter use, and general population risk for anaesthesia administration. There may also be a reduced need for community care nursing and physician follow-up after patients are discharged, because of potential improved recovery times and less post-operative morbidity.

3 Company claimed benefits and the decision problem

These are described in the scope here (link to Appendix E). Neither the company nor the EAC proposed any variation to the decision problem.

Table 1: The decision problem

Decision problem	Scope
Population	Men with lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) aged 45 or over, and with prostate volumes no greater than 100 ml
Intervention	The UroLift system in inpatient or day case setting
Comparator(s)	•Monopolar or bipolar transurethral resection of the prostate (TURP) •Holmium laser enucleation of the prostate (HoLEP) •Transurethral water vapour therapy using Rezum (NxThera Inc)
Outcomes	The outcome measures to consider include: •Length of hospital stay •The need for, or duration of, post-operative catheterisation •Number of post discharge follow-on consultations, both in primary and secondary care settings •Time to re-operation and re-operation rates •Symptoms of BPH (using the International Prostate Symptom Score [IPSS]) •Changes in ejaculatory or sexual function •Time to return to normal activities •Quality of life •Hospital-acquired infection •Theatre and staff time

	• Incidence of chronic atonic bladder, detrusor sphincter dyssynergia, chronic urinary infection, chronic renal failure • Device-related adverse events • Number of implants
Cost analysis	Comparator(s): Monopolar or bipolar TURP, HoLEP and Rezum Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be long enough to reflect differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers of implants and combinations of devices are needed.
Subgroups to be considered	Men for whom TURP or HoLEP is unsuitable because of operative risk including risks of blood loss or anaesthesia.
Special considerations, including those related to equality	Men who wish to preserve sexual function and fertility.
Special considerations, specifically related to equality	Are there any people with a protected characteristic for whom this device has a particularly disadvantageous impact or for whom this device will have a disproportionate impact on daily living, compared with people without that protected characteristic?
	Are there any changes that need to be considered in the scope to eliminate unlawful discrimination and to promote equality?
	Is there anything specific that needs to be done now to ensure the Medical Technologies Advisory Committee will have relevant information to consider equality issues when developing guidance?
Any other special considerations	Not applicable

4 The evidence

The original guidance for Urolift (MTG26; published 2015) the EAC included evidence from 9 clinical studies, on which the EAC performed their own evidence synthesis. This guidance update is based on evidence published since the original guidance was produced.

The EAC did a new evidence search using the search strategy from the original assessment report for MTG26. These searches were conducted on 14th July 2020 in the following databases: Medline ALL (Ovid), EMBASE (Ovid), Cochrane Database of Systematic Reviews, CENTRAL, HTA and NHS EED (CRD). Searches were also conducted for ongoing trials in Clinical Trials.gov, WHO International Clinical Trials Registry Platform and of the Company's website.

4.1 Summary of evidence of clinical benefit

The rational for this decision is in section Appendix C of the AR

Table 2: Studies included and excluded in the guidance update

Study	Type of publication	Type of study	Comment
Studies included by both EAC and company			
Tutrone and Schiff 2020	Full paper	Non-randomised, prospective, comparative study	Direct comparison between Urolift and Rezum
Rukstalis et al. 2018	Full paper	Non-randomised, prospective, comparative study	Study includes men with obstructing medial lobe
Royal Devon & Exeter NHS Trust 2020	Full paper	NICE shared learning case study	A prospective database search of all patients undergoing Urolift. N=93 patients in total.
Northampton NHS Trust 2020	Full paper	NICE shared learning case study	Retrospective comparison of Urolift (n=20) and for TURP (n=20)
Norfolk & Norwich NHS Trust 2019	Full paper	NICE shared learning case study	Audit data 2016-2019. Jan 2016-Sept 2016: UroLift n=72, TURP n=122, HoLEP n=115 Jan 2016-June 2019: UroLift n=250, TURP n=520, HoLEP n=490
NHS Fife 2020	Full paper	NICE shared learning case study	61 men treated with UroLift who were eligible for TURP
Studies in submission excluded by EAC			
Rochester et al (2019)		Poster presentation	indication of acute urinary retention (AUR) outside of scope
Young et al 2018	Abstract	Poster presentation	lack of reported clinical outcomes outside of scope
[redacted]	Abstract	Real-world case studies	No details available for extraction
[redacted]	Abstract	Real-world case study	[redacted] outside of scope

[redacted]	Abstract	Follow-up to [redacted] study	[redacted] outside of scope
[redacted]	Abstract	Real-world case study	No details available for extraction

Studies not in submission included by EAC			
Roehrborn et al. 2015	Full paper	Randomised control trial	L.I.F.T study
Rukstalis et al. 2016	Full paper	Randomised control trial follow up	L.I.F.T study follow-up
Roehrborn et al. 2017	Full paper	Randomised control trial follow up	L.I.F.T study follow-up
Sonksen 2015	Full paper	Randomised control trial	The BPH6 study
Gratzke et al. 2016	Full paper	Randomised control trial follow up	The BPH6 study follow-up
Bozkurt 2016	Full paper	A Retrospective non-comparative study	
Bardoli et al. 2017	Full paper	Single centre, single surgeon retrospective note analysis	
Eure et al. 2019	Full paper	Retrospective multicentre chart analysis	
Sievert et al. 2019	Full paper	non-comparative, prospective, multicentre studies	
Rubio et al. 2019	Full paper	non-comparative, prospective, multicentre studies	

NHS St Helens and Knowsley (2016)	Full paper	NICE shared learning case study	Urolift (n=7) biTURP (n=75) mTURP (n=17) HoLEP (n=6) TUIP (n=5)
NHS Frimley park (2016)	Full paper	NICE shared learning case study	Urolift (n=75) TURis (n=190) Greenlight (n=80-90)

The company submitted 12 studies (Tutrone and Schiff 2020, Rochester et al. 2019, Young et al. 2018, [redacted], [redacted] and [redacted], [redacted] and [redacted], Royal Devon & Exeter NHS Trust 2020, Northampton NHS Trust 2020, Norfolk & Norwich NHS Trust 2019, NHS Fife 2020); EAC agreed with the inclusion of 5 (Tutrone and Schiff 2020, Royal Devon & Exeter NHS Trust 2020, Northampton NHS Trust 2020, Norfolk & Norwich NHS Trust 2019, NHS Fife 2020) of these 11 and include a further 10 (Roehrborn et al. 2015, Rukstalis et al. 2016, Roehrborn et al. 2017, Sonksen 2015, Gratzke et al. 2016, Bozkurt 2016, Bardoli et al. 2017, Eure et al. 2019, Sievert et al. 2019, Rubio et al. 2019) studies.

A total of 12 studies and 4 NICE shared learning case studies were included in the ARU. These included:

- 2 RCTs reported in 5 papers: The LIFT study (reported in Roehrborn et al. 2015, Rukstalis et al. 2016 and Roehrborn et al. 2017) and the BPH6 study (reported by Sonksen 2015 and Gratzke et al. 2016)
- 2 non-randomised, comparative, prospective studies (Tutrone and Schiff 2020, Rukstalis et al. 2018)
- 2 non-comparative, prospective, multicentre studies (Sievert et al. 2019; Rubio et al. 2019)
- A retrospective non-comparative study (Bozkurt 2016)
- A single centre, single surgeon retrospective note analysis (Bardoli et al. 2017)
- A retrospective multicentre chart analysis (Eure et al. 2019)

- 4 NICE shared learning case studies (Royal Devon & Exeter NHS Trust 2020; Northampton NHS Trust 2020, Norfolk & Norwich NHS Trust 2019 and NHS Fife 2020).

The EAC concluded that most of these studies were of a moderate or high quality, including direct comparisons and appropriate patient populations. The 2 papers reporting the L.I.F.T study (Roehrborn et al. 2015 and 2017) were deemed to have a low risk of bias as both the patients and assessors were blinded to the procedures and outcomes. The EAC noted some concern of bias with BPH6 study (Sonksen et al. 2015 and Gratzke et al. 2016), as neither the patients nor the assessors were blinded to the intervention and the papers did not report whether the analysis of results used an intention to treat (ITT) approach.

The non-randomised crossover and comparative studies (Rukstalis et al. 2016, Rukstalis et al. 2018 and Tutrone and Schiff. 2020) were non-randomised but otherwise were also deemed low risk of bias.

Two of the non-comparative studies were found to be of good quality (Bozkurt et al. 2016 and Rubio et al. 2019). The other the non-comparative studies were of poorer quality, with various issues reported by the EAC. The studies by Bozkurt et al. 2016, Bardoli et al. 2017 and Rubio et al. 2019 had sample sizes of less than 20 people. The studies by Eure et al. 2019 and Sievert et al. 2019 included very limited or no inclusion criteria. Bardoli et al. 2017 did not clearly report outcome measures and none of the non-comparative studies reported whether any blinding of the intervention was included.

The EAC noted that most of the evidence was from studies that were not conducted in the NHS. The BPH6 Study (Sonksen et al. 2015 and Gratzke et al. 2016) was a multicentre study that included sites in the UK as well as other European countries. The Bardoli et al. single centre retrospective analysis was the only study that was done solely in the UK. The EAC regarded that the results from the non-UK studies may not be readily generalisable to the NHS.

Table 3: Key clinical evidence included in the guidance update

Study and design	Participants/ population	Intervention & comparator	Outcome measures and follow up	Results	Withdrawals	Funding	Comments
Roehrborn et al. 2015 L.I.F.T RCT 3-year follow-up study, only reporting follow-up data in PUL group compared to baseline	206 male participants, Diagnosis of symptomatic BPH, Age ≥ 50 years	**Intervention**: Active PUL (UroLift) **n** = 140, mean age 67 years (93 included for effective analysis at 3 years) **Control**: Sham procedure **n** = 66, mean age 64 years Outcomes for the control group not reported in this follow-up study	Three-year follow-up: • IPSS score • IPSS QoL score • BPHII: BPH Impact Index • Peak flow rate (Qmax) • Sexual function (SHIM: Sexual Health Inventory for Men and MSHQ-EjD: Male Sexual Health Questionnaire for Ejaculatory Dysfunction) • Adverse events	**In PUL group, compared to baseline:** **IPSS:** Percentage decrease from baseline to 3-years of 41.1%, p<0.0001 **IPSS-Quality of life (QoL):** Percentage change from baseline to 3-years decreased 48.8%, p<0.0001 **BPH Impact Index (BPH II):** Percentage change from baseline to 3-years was decreased 53.2%, p<0.0001 **Qmax**: percentage increase from baseline to 3-years of 53.1%, p<0.0001 **PVR**: percentage change not significantly different. **SHIM**: No significant differences in change in SHIM score from baseline and 3 year follow-up	36 not included in analysis (11 lost to follow-up)	Not reported	Randomisation procedure used permuted blocks of various sizes chosen at random through a password protected electronic database Study was powered for the primary endpoint assuming a t-test comparison of mean values with 0.5 two-sided type 1 error and 80% statistical power

				MSHQ-EjD function change was 8.9% from baseline (p=0.0129) and MSHQ-EjD Bother change was -27.4% from baseline (p=0.0002) to 3 years. Operation time was 66.16 minutes for UroLift compared to 46.86 minutes for the sham procedure. Mean number of implants was 5.2 Time to discharge was 0.19 days for UroLift and 0.16 days for the sham procedure. 32% of UroLift patients required catheterisation with an average 0.9 catheterisation days reported for the cohort as a whole			

Rukstalis et al. 2016 Open-label, crossover study looking at 24-month durability after crossover to PUL following blinded control sham procedure in the L.I.F.T study. After 3 month follow-up, patients were unblinded and offered enrolment in crossover study during which they received PUL treatment and were	51 men who had previously undergone a sham procedure as part of the L.I.F.T study (mean age 64 years)	PUL (UroLift)	**3-month post sham outcomes**: • IPSS • Qmax • IPSS QoL • BPH II • PVR • SHIM questionnaire **24 month outcomes after cross-over to PUL**	Significant improvement in **BPHII** from baseline to 1 month (change from 7.33 to 3.24), 3 months (7.32 to 2.94), 6 months (7.33 to 2.84), 12 months (7.43 to 3.43) and 24 months (7.12 to 3.19), all p <0.001. Significant improvement for **MSHQ-EjD** from baseline to 1 month (change from 8.71 to 11.56) 3 months (8.86 to 11.19), 6 months (8.82 to 11.11), 12 months (8.88 to 10.94) and 12 months (8.94 to 10.65), all p <0.001. Significant improvement in **IPSS** scores from baseline to 0.5 months (change from 25.41 to 18.92), 1 month (25.41 to12.43), 3 months (25.44 to 12.32), 6 months (25.41 to 13.06), 12 months (25.49 to 15.22) and 24 months (24.76 to 15.17), all p <0.001. Significant improvement in **Qmax** from baseline to 3 months (7.95 to 11.95), 12 months (8.09 to12.07) and 24 months (8.00 to 12.18),	3	NeoTract Inc	Funded by manufacturer

followed by 24 months.				all p <0.001 Significant improvement in **PVR** from baseline to 3 months (change from 89.26 to 52.95, p=0.003) and 12 months (87.98 to 56.74, p=0.004). No significant difference found at 24 months compared to baseline (86.55 to 79.23). Significant improvements in **IPSS QoL** from baseline to 0.5 months (change from 4.80 to 3.43) 1 month (4.80 to 2.35), 3 months (4.78 to 2.18), 6 months (4.80 to 2.45), 12 months (4.78 to 2.73) and 24 months (4.64 to 2.64), all p <0.001. Anaesthesia time was 51.25 minutes Mean number of implants was 4.5 Time to discharge was 0.21 days			

Roehrborn et al. 2017 L.I.F.T study – 5-year follow-up	87/140 patients were available from the PUL group at 5 years. 96 patients available at 49-60 months. Mean age not reported. Missing data at 5 years was imputed using last observation carried forward.	PUL (UroLift)	60 month follow-up: • IPSS • IPSS-QoL • Qmax • BPHII • MSHQ-EjD	Significant improvement in **BPHII** from baseline (6.92) to 5-year follow-up (3.51, p<0.0001) Significant improvement in **IPSS** from baseline (22.32) to 5-year follow-up (14.47, p<0.0001) Significant improvement in **Qmax** from baseline (7.88) to 5-year follow-up (11.08, p<0.0001) Significant improvement in **IPSS QoL** from baseline (4.62) to 5-year follow-up (2.54, p<0.0001)	36 not included in analysis		Reporting of sample size is inconsistent throughout
Rukstalis et al (2018) 12 month follow-up from MedLift study. This was a cohort extension of the L.I.F.T study looking at only those	Intervention: n=45 patients enrolled from 71 identified from the L.I.F.T study Additional comparative analysis: n=181 for IPSS at 3 months.	Intervention: UroLift treatment of obstructive median lobe (OML group) Additional comparative analysis: UroLift in a group that included both	12-month follow-up: • IPSS • QoL • BPH-II • Qmax • IIEF • MSHQ-EjD • SHIM • Adverse events	**BPH Impact Index (BPH II)** OML group: significant decrease from baseline (7.7) and 1 month (3.7), 3 months (1.8), 6 months (1.7) and 12 months (2.1), all p<0.0001 Combined group: significant decrease from baseline (7-7.1) and 1 month (3.9), 3 months (2.6), 6 months (2.4) and 12 months (2.6),	0	Funding: NeoTract/Teleflex Inc.	The study was powered to have 95% probability of establishing the true percent improvement in IPSS score from baseline to 6 months was

with obstructive medial lobe (OML) See Roehrborn et al (2015) **USA**	See Roehrborn et al (2015)	lateral lobe (LL) patients from the L.I.F.T. study and the OML patients from the intervention arm (Combined group)_		all p<0.0001 The size of the % change was significantly bigger in the OML group compared to the combined group at each time point (p=0.05-0.0007) **MSHQ-EjD** OML group: significant increase from baseline (9.2-9.4) and 1 month (11.4), 3 months (11.3), 6 months (11.2) and 12 months (11.4), all p<0.0026 Combined group: significant increase from baseline (8.9-9) and 1 month (11.3), 3 months (11.1), 6 months (10.7) and 12 months (10.6), all p<0.00001 The size of the % change did not differ between groups at any time point **IPSS:** both groups showed similar, significant decreases from baseline at 1, 3, 6 and 12 months. **IIEF:** OML group: no significant difference in			greater than 25%, with 95% confidence. The minimum required number of evaluable subjects was determined to be 35. Funded by manufacturer

				scores from baseline (21.8 - 22.5) to any time-point. Combined group: significant increase from baseline (20.5 - 21.0) and 1 month (22.0) and 3 months (22.2), p=0.02 and 0.004 respectively. No significant differences at 6 months and 12 months. **SHIM:** OML group: significant increase from baseline (17.2-17.6) and 3 months (18.7) and 12 months (18.4), p=0.05 and 0.04 respectively. No significant differences were found between baseline and 1 and 6 months. Combined group: significant increase from baseline (16.4-16.7) and 1 month (17.6), 3 months (17.8), and 12 months (17.2), p=0.002-0.05. There was no significant difference at 1 month. **IPSS:** OML group: significant decrease from baseline (24.1-24.2) and 1 month (9.8), 3 months (8.3),			

				6 months (10.0) and 12 months (10.6), all p<0.0001 Combined group: significant decrease from baseline (22.7-22.8) and 1 month (11.7), 3 months (10.4), 6 months (10.9) and 12 months (11.3), all p<0.00001 The % change was significantly bigger in the OML group compared to the combined group at every time point, especially 1 and 3 months (p=0.03-0.0003) **Maximum urinary flow rate (Q_{max} (mL/s)) and postvoid residual volume (PVR (mL))** OML group: scores significantly increased from baseline (7.1-7.2) compared to 1 month (15) 3 months (14.6), 6 months (12.3) and 12 months (13.5), all p<0.0001 Combined group: significant increase from baseline (7.1-7.8) and 1 month (15), 3 months (12.9), 6 months (12.3) and 12 months (12.5), all p<0.00001			

				Differences in % change was only reported for 3 and 12 months and was significantly bigger in the OML group at 3 months only (p=0.002) **IPSS-Quality of life (QoL)** OML group: QoL scores significantly decreased from baseline (4.9) compared to 1 month (1.8), 3 months (1.6), 6 months (1.9) and 12 months (1.9), all p<0.0001 Combined group: significant decrease from baseline (4.7) and 1 month (2.4), 3 months (2.2), 6 months (2.1) and 12 months (2.2), all p<0.00001 The % change was significantly bigger in the OML group than the combined group at every time point, (p=0.01-0.0003) except at 6 months where no difference was found. Mean length of stay was 2.4 hours Mean number of implants was 6.3			

				Catheterisation rate and length (mean days) 29/45 (64.4%) were catheterised post-operatively. A further 7 (15.6%) required catheterisation prior to discharge. Mean duration of catheterisation was 1.2 days			

Sonksen 2015 The BPH6 study Multicentre, prospective, randomised controlled trial at 10 European centres: Denmark UK Germany Italy	80 men with LUTS secondary to BPH • Male aged ≥50 yr • International Prostate Symptom Score >12	**PUL (UroLift) n** = 45 (46 randomised, 1 declined treatment), 44 included in analysis, mean age 63 years. **TURP n** = 35 (45 randomised, 10 declined treatment), mean age 65 years	Primary study endpoint was a composite of 6 elements that assess overall outcome One-year follow-up: • IPSS score • Quality of Recovery visual analogue score (QoR VAS) • Sexual Health Inventory for Men (SHIM) • MSHQ-EjD • Incontinence Severity Index (ISI) • Adverse events	**BPH Impact Index (BPH II):** No significant differences between UroLift and TURP at any of the follow-up time points **Incontinence (ISI): People i**n the TURP group had a significant worsening at both 2 weeks and 3 months. No values given. Continence preservation was comparable between the groups, and no patient experienced new-onset stress or sphincter incontinence. Of the participants who failed the BPH6 continence element (six PUL and eight TURP patients had ISI > 4 at any time), none of the PUL patients reported new-onset pad use, whereas 6 TURP patients (6/8, 75%) reported that they required pads after TURP (superior PUL performance, p = 0.01). **Erectile and sexual dysfunction (MSHQ,**	1 from TURP group and 1 from UroLift group (note that the numbers stated in the prisma diagram are not consistent)	NeoTract Inc.	The study was powered to establish noninferiority of PUL to TURP for noninferiority delta of 10% for the BPH6 primary endpoint. Performance estimates from the literature predicted that power of 80% would be achieved with enrolment of 62 participants, assuming the BPH6 success rate was 51% and 30% for PUL and TURP, respectively. Parallel randomization was conducted at a ratio of 1:1 at the time of the procedure,

				MSHQ-EjD, IIEF and SHIM): No significant differences in change in SHIM score from baseline UroLift and TURP at any of the follow-up time points. Significant differences in MSHQ-EjD function at 1 month (UroLift change from 10.6 to 12.3 and TURP 8.6 to 7.7, p = 0.03), 3 months (UroLift 10.3 to 11.5 and TURP 9.3 to 6.3, p = 0.0002), 6 months (UroLift 10.8 to 11.9 and TURP 8.9 to 5.7, p <0.0001) and 12 months (UroLift 10.6 to 11.9 and TURP 9.3 to 5.6, p <0.0001). No significant differences for MSHQ-EjD bother at 1, 6 and 12 months. Significant differences at 3 months (UroLift 1.7 to 1.1 and TURP 1.9 to 2.1, p = 0.01). **IPSS:** No significant differences between UroLift and TURP at 2 weeks, 1, 3 and 6 months. At 12 month follow-up, UroLift score (10.7) was			stratified by site, and performed using permuted blocks of various sizes chosen at random and concealed through a password-protected computer database

				significantly higher than TURP (7.3), p=0.02 **Maximum urinary flow rate (Q_{max} (mL/s)) and postvoid residual volume (PVR (mL))**: Significant differences in change from baseline in Qmax at 3 months (UroLift change from 9.4 to 13.6 and TURP 9.2 to 22.6, p <0.0001), 6 months (UroLift 9.6 to 13.5 and TURP 9.4 to 19.0, p=0.003) and 12 months (UroLift 9.6 to 13.6 and TURP 9.5 to 23.2, p <0.0001). Significant differences in change from baseline in PVR at 3 months (UroLift change from 87.6 to 77.3 and TURP 98.6 to 47.6, p=0.002), 6 months (UroLift 85.5 to 80.7 and TURP 100.5 to 46.2, p = 0.003) and 12 months (UroLift 86.3 to 93.7 and TURP 103.5 to 33.6, p = 0.002). **IPSS-Quality of life (QoL):** No significant differences between UroLift and TURP			

				at any of the follow-up time-points Time to discharge was 1.0 days for UroLift compared to 1.9 days for TURP Mean number of implants was 4.7 Anaesthesia time was 55 minutes for UroLift and 71 minutes for TURP **Catheterisation rate and length (mean days):** 74% of the TURP group required catheterisation for >24 hours compared to 45% of the UroLift group (p=0.01)			

Gratzke et al. 2016 **The BPH6 study.** Prospective, randomised, controlled, non-blinded study at 10 European centres in 3 countries Germany UK Denmark	80 patients were randomised 1:1 to either PUL (UroLift) or TURP. Number of patients randomised to each group not reported. Number of patients contributing data to each outcome reported. From Sønsksen et al. (2015) 45 in PUL arm and 35 in TURP arm (BPH6 study).	**PUL (UroLift) n** = 45, mean age 63 years **TURP n** = 35, mean age 65 years	**Two-year BPH6 follow-up:** • IPSS score • Sexual Health Inventory for Men (SHIM) • MSHQ-WjD • Incontinence Severity Index (ISI) • Adverse events	No significant differences between groups at any follow-up for any of the following: BPH Impact Index (BPH II), SHIM, MSHQ-EjD bother, IPSS(QoL) Average ISI score was consistent throughout follow-up for the UroLift group and did not change significantly from baseline at any time point. No figures or p-values were given. Significant differences in change in MHSQ-EjD function from baseline to 1 month (UroLift 10.6 to 12.3 and TURP 8.6 to 7.7, p=0.049), 3 months (UroLift 10.8 to11.5 and TURP 9.3 to 6.3, p <0.001), 6 months (UroLift 10.8 to 11.9 and TURP 8.9 to 5.7, p <0.001), 12 months (UroLift 10.6 to 11.9 and TURP 9.3 to 5.6, p <0.001) and 24 months (UroLift 10.6to 10.9 and TURP 8.9 to 4.9, p <0.001). Significant differences in the change in IPSS scores from baseline between groups at	1 from TURP group and 1 from UroLift group	Not reported	Sample size and n's reported for each group do not match

				12 months (UroLift 21.8 to 10.9 and TURP 22.8 to 7.3, p=0.013) and 24 months (UroLift 21.4 to 12.2 and TURP 22.8 to 7.4, p = 0.004). Significant differences between groups in the change in baseline for Qmax at 3 months (UroLift 9.4 to 13.6 and TURP 9.0 to 21.7, p<0.001), 6 months (UroLift 9.6 to 13.5 and TURP 9.4 to 19.0, p=0.003), 12 months (UroLift 9.6 to 13.6 and TURP 9.5 to 23.2, p<0.001) and 24 months (UroLift 9.3 to 14.3 and TURP 9.6 to 25.5, p=0.002). Significant differences in the change from baseline in PVR at 3 months (UroLift 87.6 to 77.3 and TURP 98.6 to 47.6, p = 0.014), 6 months (UroLift 85.5 to 80.7 and TURP 100.5 to 46.2, p = 0.009) and 12 months (UroLift 86.3 to 93.7 and TURP 103.5 to 33.6, p <0.002). No significant difference was seen at 24 months.			

Tutrone and Schiff 2020 USA Non-randomised, prospective, comparative study across two study sites	53 male patients: **Inclusion criteria:** • Undergone either UroLift or Rezum procedure within the last 2 months. • Urolift indicated for men aged ≥ 45 and prostates ≤ 100 cc ith no lower limit. • Rezum indicated for men ages ≥ 50 and prostates ≥ 30 cc and ≤ 80 cc. **Exclusion criteria:** • None	**Intervention**: UroLift n=30 (mean age 68 years; prostate volume 49cc) **Comparator**: Rezum n = 23 (mean age 69 years; prostate volume 63cc)	Questionnaires completed an average of 30 days post procedure • IPSS • IPSS QoL • SHIM • MSHQ-EjD • MSHQ-EjD (bother)	SHIM scores were significantly higher in the UroLift group (14.8) compared to Rezum (9.2), p=0.02. MSHQ-EjD scores were significantly higher in the UroLift group (12.2) compared to Rezum (9.2), p=0.04. There was no significant differences between groups for MHSQ-EjD bother scores. IPSS scores were significantly higher in the Rezum group (15.6) compared to UroLift (8.6), p=0.001. IPSS QoL scores were significantly higher in the Rezum group (2.5) compared to UroLift (1.5), p=0.04. 57% of UroLift compared to 87% of Rexum patients required post procedure catheterisation (p=0.03)	0	Sponsored by the manufacturer	Relatively low sample sizes

				Mean duration of catheterisation was 1.2 days for UroLift and 4.5 days for Rezum (p=0.0004)			
Abbreviations: IIEF: International Index for Erectile Function; IPSS: International Prostate Symptom Score; IPSS QoL: International Prostate Symptom Score – Quality of Life; MSHQ-EjD: Men's Sexual Health Questionnaire – Ejaculatory Dysfunction; PVR: Post-void Residual; Qmax: Maximum urinary flow rate; SHIM: Sexual Health Inventory for Men;							

The clinical evidence reviewed by the EAC suggested that UroLift is beneficial to patients compared to other procedures, and improvements are maintained over time:

- BPH-II scores consistently improved over time and remained so up to 5 years post procedure (Roehrborn et al. 2015, Rukstalis et al. 2016 and Roehrborn et al. 2017, Rukstalis et al. 2018).

- IPSS results showed significant improvements in symptom severity compared to baseline for UroLift patients up to 5-years post procedure (Roehrborn et al. 2015, Bozkurt et al. 2016, Rukstalis et al. 2016, Bardoli et al. 2017, Roehrborn et al. 2017, Sievert et al. 2018, Eure et al. 2019 and Rubio et al. 2019, Rukstalis et al. 2018).

- Changes in erectile and sexual dysfunction measures (MHSQ-EjD, IIEF and SHIM) varied between studies. The IIEF and SHIM questionnaires, (a shortened version of the IIEF) both focus specifically on erectile dysfunction. UroLift patients did not show significant improvements in these measures over time in the majority of studies (Bozkurt et al; 2016, Rukstalis et al; 2016 and Rubio et al; 2019). However, Rukstalis et al (2018) looked specifically at patients with obstructing medial lobes and showed improvements in both of these measures up to 12 months follow-up. Five studies reported MSHQ-EjD bother scores with 2 showing improvements over time (Roehrborn et al; 2015 and Rukstalis et al; 2018), 2 showing no significant differences in improvement over time when compared to TURP (Sonksen et al; 2015 and Gratze et al; 2016) and 1 showing no significant difference between UroLift and Rezum patients at 30 days follow-up (Tutrone and Schiff, 2020).

- Urological outcomes, Qmax and PVR, were measured in 11 of the 12 included clinical studies. In most of these, Qmax values improved following Urolift treatment and up to 5-years follow-up (Roehrborn et al; 2015, Bozkurt et al; 2016, Rukstalis et al; 2016, Roehrborn et al; 2017, Rukstalis et al; 2018, Sievert et al; 2018 and Rubio et al; 2019. Eure et

al. 2019 reported that Qmax scores decreased over time up to 6 months follow-up, and Bardoli et al (2017) showed no significant differences across time. Six studies reported PVR values, 4 of which showed a significant improvement up to 24 months for UroLift patients (Bozkurt et al; 2016, Rukstalis et al; 2016, Bardoli et al; 2017, Sievert et al; 2018). Gratzke et al (2016) reports that ISI scores for incontinence remained consistent for UroLift patients up to 2-years follow-up.

- Eleven studies used QoL measures with 8 showing a significant improvement across time up to 5-years when using UroLift.

- One study comparing UroLift with TURP and another comparing UroLift and Rezum reported catheterisation rates were significantly reduced for UroLift patients. In addition, UroLift patients who were catheterised, were so for significantly less time, compared to both TURP (Sonksen et al; 2015) and Rezum (Tutrone and Schiff; 2020).

- Only the study comparing UroLift with TURP reported hospitalisation times, and these were significantly reduced for UroLift patients (Sonksen et al; 2015).

The evidence indicates that Urolift improves BPH symptoms over time, but that the magnitude of improvement is lower than those seen for TURP in symptom severity and urological outcomes. When compared to TURP, people treated with UroLift had significantly less improvement in IPSS scores up to 12 months post procedure (Sonksen et al;2015 and Gratzke et al; 2016). The amount of change in SHIM scores, BPH-II scores, and the erectile dysfunction SHIM scores did not differ significantly between UroLift and TURP patients (Sonksen et al; 2015 and Gratzke et al; 2016). 2 studies showed that changes in MSHQ-EjD Function scores over time were significantly better for UroLift patients than people who had TURP (Sonksen et al; 2015 and Gratzke et al; 2016). 2 studies showed that people who had TURP showed significantly greater improvements in Qmax scores up to 24 months follow-up than people who had UroLift (Sonksen et al; 2015 and Gratzke et al; 2016). People having

TURP also had significantly greater improvements in PVR values compared to those who had UroLift (Sonksen et al, 2015 and Gratzke et al; 2016). Incontinence measures (ISI questionnaire) were only included in 2 studies; Sonksen et al (2015) showed significantly worse scores for TURP patients at 2 weeks and 3 months when compared to UroLift patients. Sonksen et al (2015) and Gratzke et al (2016) showed no significant difference in quality of life scores between people having TURP and UroLift, up to 12 and 24 months respectively.

The EAC noted that UroLift appeared to be superior to Rezum for improving BPH symptom severity and erectile dysfunction measures. The study by Tutrone and Schiff (2020) compared Urolift to Rezum. They reported that people treated with Urolift had significantly better IPSS scores, better SHIM scores, and significantly better MSHQ-EjD Function scores over time. QOL scores for people treated with UroLift were significantly better than for people treated with Rezum. Outcomes were reported at approximately 30 days post procedure.

Tutrone and Schiff (2020) compare Urolift to Rezum and Sonksen et al (2015) compare Urolift to TURP. Using these studies to compare the 3 interventions, the outcomes of people treated with UroLift, TURP and Rezum at 30 days or 1month post-surgery are mixed. For symptom severity (IPSS), UroLift patients score best, followed by TURP then Rezum. SHIM scores show UroLift patients scoring highest, followed by TURP then Rezum. For the MSHQ-EjD, UroLift patients again score highest but followed by Rezum then TURP patients. Finally, for QoL scores, UroLift again scores highest, followed by Rezum then TURP. As the Tutrone study does not compare to baseline, the EAC could not comment on the size of improvements.

Treatment of people with obstructing median lobe (OML) has been added as a new indication in the update to the Urolift guidance. The comparative results from Rukstalis et al; 2018 have not been discussed in full as the comparator is outside of scope. However, the results do show that UroLift is as beneficial for patients with OML in relation to symptom severity, ejaculatory and erectile

dysfunction, urological and quality of life measures, when compared to lateral lobe (LL) patients who took part in the L.I.F.T study.

In conclusion, the results are mixed and do not show that UroLift is superior when compared to TURP for urological, QoL or symptom severity outcomes. However, UroLift does appear to be superior to Rezum for erectile dysfunction and symptom severity outcomes. In addition, when looking at outcomes over time, UroLift does appear to improve patient's symptoms over a long timeframe.

As the original assessment report (Ray et al, 2015) and UroLift guidance (MTG 26) did not include any comparison data, the results comparing with TURP and Rezum from this update cannot be compared. The studies included in this update show a similar pattern of results for Urolift as were described in the original guidance; improvements in symptom severity measures, urological outcomes and quality of life measures.

4.2 Summary of economic evidence

The company's submission did not include any economic studies. The EAC did a literature search in July 2019 using the search strategy from the AR for the original guidance. This search identified 1 published cost effectiveness model (Ulchaker & Martinson 2018), 1 cost equivalence study (DeWitt-Foy et al 2019) and 1 related review (Gill et al. 2018) that included cost information from the main literature search for the topic.

The cost effectiveness model (Ulchaker & Martinson 2018) found that Urolift was dominated by Rezum, being more expensive and less effective. The cost equivalence study found Urethral Lift to be more expensive to provide than any of the other techniques considered except open or robotic prostatectomy (De Witt –Foy et al. 2019). These studies were not included in the company submission, and they are not of direct relevance as they are set in the US. De Witt-Foy note that their results are very different from studies in Europe for TURP and medication, and differences are likely to be apparent across all therapies.

De novo analysis

The company created a de novo cost consequence model using Treeage software. The model is described in section 10.1 of the company's submission.

The de novo model is broadly based on the decision tree model used for the original guidance but with the addition of Rezum added as a comparator and the inclusion of the new Urolift indication of median lobe treatment.

The new model includes branches for success (symptom relief) or failure, and both branches may be with or without incontinence.

There is no Markov element included in the model, no discounting and no consideration of mortality. The original model (MTG26) included 3.5% discounting for a 2 - year time horizon.

Model parameters

Costs and resource use

The costs used in the cost model in the original guidance, the de novo economic model submitted for the guidance update, and changes made by the EAC are described in table 4. Sources of the costs data and comments from the EAC are also included. Please see the ARU for a full description of the cost and clinical parameters used in the economic model and the EAC's amendments to it.

The EAC highlighted the following changes to the de novo cost model compared with the cost model used in the original guidance:

- The time horizon has been extended from 2 to 5 years, which impacts on the cost of incontinence over that period and the rate of failure selected for Urolift (this is a fixed rate within the model, but dependant on the time horizon chosen)
- Capital costs have been removed from the current model, this has very little impact on the overall result
- Consumables costs have been updated to 2019, and in addition the costs for mTURP and biTURP now include additional items based on calculations in MTG29 and MTG49. There is some variation between the guidance documents on how these calculations should be interpreted. The EAC have changed the submitted company model parameter to be in line with the accepted calculation method in MTG49
- The following costs have been removed from the model submitted by the company for the guidance update: pre procedure outpatients consultation, pre and post procedure tests, fluids and other consumables during procedures. These were the same for all procedures, so removing them is appropriate and reduces costs for all procedures equally.

Table 4. Costs used in the economic model for Urolift in the original guidance, in the company's submission for the guidance update, and changes made by the EAC

Item	Cost used in AR model for original 2015 guidance (source)	Cost used in submission for 2020 guidance update (source)	EAC updates to costs	Comments
Cost of Adverse Events: **AUR treatment (c_compRet)**	£2, 683 Annemans 2005	£3,061.79 Rezum Medical Technology Guidance 2020 (MTG49) – Inflated to 2019 from Annemans 2005	**£3,061.79**	No change
Cost of Adverse Events: **Stricture (c_compStric)**	£550.99 54% at £373.60 day case, NHS National Schedule of Reference Costs, 2013-14.TDC. Code LB15E, Minor Bladder Procedures, 19 years and over + 46% at £759.23, inpatient NHS National Schedule of Reference Costs, 2013-14. EI. Code LB15E, Minor Bladder Procedures	£504.84 68% at £309; NHS Ref costs 2017-18; Day case HRG LB15E Minor bladder procedures, 19 years and over + 32% at £921 NHS Ref costs 2017-18; Elective inpatient HRG LB15E Minor bladder procedures, 19 years and over.	**£520.40 using 68%:32% split.**	Using 54%:46% split would give £596.70 Updated costs using NHS Ref costs 2018-19. The EAC have used the submitted % split, but highlight that it has not been justified by the company. In previous guidance MTG49 the cost was £330, there is no explanation given for why these have changed. MTG49 Rezum used £330 which is the total HRG average cost for NHS ref costs 2017-18
Cost of Adverse Events: **Transfusion (c_compTrans)**	£329 £121.85 per unit RBC NHS price list	£348 Updated cost from MTG26	**£348**	£128.99 per unit RBC NHS price list 2018/19, 2.7 units. This is in line with previous accepted

	2014/15, 2.7 units. Used in EAC base case (original model used £862, NICE 2010)	[Actually included in submitted model as £357.95]		costs, but does not include costs of delivering the transfusion.
Cost of Adverse Events: TUR (c_compTURS)	£1,875.36 2 days in high dependency ward (£643.00) CCSALCCU. Code XC07Z, Adult Critical Care, 0 Organs Supported and 2 days in normal ward (294.36)EI_XS. Code LB25F, Transurethral Prostate Resection Procedures with CC Score 0-2 NHS reference costs 2013/14	£2,102 2 days in high dependency ward (£693.00) and 2 days in normal ward £358.00 NHS reference costs 2017-18	**£2,500**	Update using NHS Ref costs 2018/19: £883 for 2 days, XC07Z Adult critical care. £367 for 2 days, normal ward, inflated to 2019 from £358 as reference cost no longer available.
Cost of Adverse Events: UTI_(c_compUTI)	£47.48 for Urolift: 1 x £45.64, GP visit PSSRU 2014 + 1 x £1.84, 10 days antibiotic BNF 2014	£781 Updated from MTG26 NHS reference costs 2017/2018 LA04S	**£738** **updated model, 2018/19 NHS Ref costs**	Updated model assumes same cost for both Urolift and comparators, which is conservative compared to previous model. Uses total HRG for LA04S, NHS ref costs 2018/19

	£709.14 for other procedures: 0.1 x £367.69, NHS Ref Cost 2013/14 LA04G UTI 1 day + 0.9 x £747.08, NHS Ref Cost 2013/14 NEI-Short stay. Code LA04M		**[Alternative: £935.6]**	If using costings from original model, this would be: 0.9 x £257 LAO4S, day case 0.1 x £1,011 LA04M, NEI-short stay (NHS Ref costs 2018/19)
Cost of Adverse Events: **Incontinence (c_incont) (per year)**	£2,425.57, year 1 £2,184.55, year 2 Complex calculation with 95% of patients receiving medication plus incontinence products, 5% of patients treated with AUS implant.	£2,356.97 Inflated cost from MTG26; used in Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation	**£10,641.84**	£2417.47 per year For 5 years = £12,087.35 With 3.5% discount = £10,641.84 Submitted costs are inflated from original model. EAC inflated to 2019 to give £2417.47, or £12,087.35 Scenario using discount at 3.5% for 5 years using CPI Health Index.
Device capital costs per procedure: Urolift	£2.50 £5,199 with 250 uses per year over 10 years	£0 Device is free of charge with consumables contract	**£0**	No change
Device capital costs per procedure: Rezum	n/a	£0	**£0**	No change
Device capital costs per procedure: TURP	£0 Equipment assumed already available	£0	**£0**	No change
Device capital costs per procedure: HoLEP	£80.59	£0	**£0**	No change

	£167,555 with 250 uses per year over 10 years			
Procedure consumables: Number of Urolift devices used per procedure (DevicesUsed)	4	3.5 Source: Data on file. [redacted] Also verified by local audits carried out by NHS users [NHS Fife 2020; [redacted]; Royal Devon & Exeter NHS Trust 2020; Norfolk & Norwich NHS Trust 2019]	**3.5**	No change
Procedure consumables: Urolift device, each (c_deviceprice)	£330.00 Neotract	£[redacted] Company	[redacted]	Cost submitted by company for update in 2019 [redacted]
Procedure consumables: Bipolar TURP consumable (c_consumablesBTURP)	£52.50 NICE 2010, clinical expert opinion (assumed same as MTURP)	£256.74 Source: NICE MTG 29 Greenlight Laser Bi-TURP includes: 1 Bi-Loop per surgery, unit cost £189.34 plus 4 bags of glycine fluid, unit cost of £5.34, plus 0.5 roller ball3333333 pieces per surgery, unit cost £50 1 Ellik evacuator per patient, unit cost £21.04	**£226.86**	Figure does not appear in any guidance or supporting docs, but method taken from MTG29 and MTG49. Figure used is manufacturer submission MTG49. Does not include glycine or roller ball. Taken individual prices from 2016 and inflated to 2019 using CPI Health. Glycine and roller ball not included, in line with MTG49 Prices for TURP consumables were based on expert opinion in 2016 and have been interpreted differently between guidelines.

		No capital or servicing costs		
Procedure consumables: HoLEP consumable (c_consumablesHoLEP)	£664.63 NICE 2010, SIGMACON supplier	£448 Blended technology cost used in Rezum Medical Technology Guidance 2020 (MTG49) – Supporting Documentation	**£448**	No change
Procedure consumables: Monopolar TURP consumable (c_consumablesMTURP)	£52.50 NICE 2010, clinical expert opinion	£88.44 From NICE MTG29 for Greenlight laser Mono-TURP includes: 1 Mono-Loop per surgery, unit cost £52.60, plus 4 bags of glycine fluid, unit cost of £5.34, plus 0.5 roller ball pieces per surgery, unit cost £50 1 Ellik evacuator per patient, unit cost £21.04 No capital or servicing costs	**£129.40**	As above for BiTURP, including all items listed by company, in agreement with MTG49.
Procedure consumables: Rezum single use treatment set (C_consumablesRezum)	Not included as comparator in original model	£1,348 Rezum Medical Technology Guidance 2020 (MTG49)	**£1,348**	No change
Staff Costs: Anaesthetist (per min)	£1.65	£1.82	**£1.82**	No change

	£99 per contact hour, PSSRU 2013	PSSRU 2019. Table 14. Hospital-based doctors. Cost per hour = £109		
Staff Costs: Band 5 nurse (per min)	£1.40 £84 per contact hour, PSSRU 2013	£1.53 PSSRU 2019. Table 13. Hospital-based nurses. Band 5 nurse. Cost per hour patient contact = £92	**£1.53**	No change
Staff Costs: Healthcare assistant (per min)	£0.35 £21 per hour, PSSRU 2013	£0.36 Urolift update. EAC used £21.40 per hour (p7 of 15). Band 2 costs not available in PSSRU	**£0.37**	Inflated to 2019
Staff Costs: Surgeon (per min)	£1.65 £99 per contact hour, PSSRU 2013	£1.82 PSSRU 2019. Table 14. Hospital-based doctors. Cost per hour = £109	**£1.82**	No change
Other procedure costs: Inpatient stay (per day) (c_LOS_hospital)	£344 Excess bed day cost is calculated from the HRG code for TURP, minus the procedure costs included in the model	£370.32 Accepted cost in Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation	**£365**	Cost given in Rezum EAC AR 2019.
Other procedure costs: Number of extra Urolift implants: obstructive median lobe (c_medianLobe)	Not included in original model	1.3 Number of extra implants used in Medlift study [Rukstalis 2019]	**1.3**	No change
Other procedure costs: Operating theatre per min (c_room_theatre)	£5.23 NICE CG97 Urology operating theatre	£14 PLICS 2016-17	**£14.60**	EAC: ISD Scotland cost book 2019, average hourly cost for theatres (urology) includes staff

	cost of £9 per minute inflated to 2014, costs subtracted for staff time.			
Follow up costs: Outpatient consultant consultation (c_visit_OPconsultant)	£99.16 NHS National Schedule of Reference Costs, 2013-2014. Table OPATT,	£112 National Schedule of Reference Costs 2017/18; Urology O/P - consultant led	**£110**	Total outpatient attendances, Urology, consultant led. NHS Ref costs 2018/19
Follow up costs: Outpatient nurse consultation (c_visit_OPnurse)	Not included in original model	£94 Source: National Schedule of Reference Costs 2017/18; Urology O/P - non-consultant led	**£88**	Total outpatient attendances, Urology, non-consultant led. NHS Ref costs 2018/19
Follow up costs: nurse led telephone consultation (c_visit_telephoneconsult)	Not included in original model	£15.70 Estimate based on 20 mins specialist nurse (Band 6). £47/hour. Source: Unit Costs of Health and Social Care. Personal Social Services Research Unit 2019	**£37.67**	20 mins specialist nurse (Band 6). £47/hour. PSSRU 2019 OR £113 patient facing hour
Follow up costs: Outpatient visit for a trial without catheter (C_visit_TWOC)	£316.23 NHS National Schedule of Reference Costs, 2013-14. OPPROC, code: EA36H Catheter with CC score 0-1' (none actually included in original model)	£144 Procedure code OPCS M47.3 Removal of urethral catheter from bladder. Maps to HRG LB15E. National Reference cost (2017/18) – Outpatient procedure (OPROC): £144	**£135**	HRG LB15E. National Reference cost (2018/19) – Outpatient procedure (OPROC)

Table 5. Resource use parameters for Urolift and comparators: length of stay post-procedure (days)

Description	Cost used in AR model for original 2015 guidance (source)	Cost used in submission for 2020 guidance update (source)	EAC updates to costs	Comments
Length of stay: bipolar TURP (LOS_BTURP)	2.63	2.33 Source: Original NICE Guidance (EAC report p75). Same LOS was used in the more recent Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation	2.63	This is the figure in the manufacturer submission and used in the model. Lourenco et al. 2008. Possibility that biTURP can now be done as day surgery (expert opinion from PLASMA update) this would reduce LOS – explored in scenario.
Length of stay: HoLEP (LOS_HoLEP)	1.98	1.98 Source: Original NICE Guidance (EAC report p75). Same LOS was used in the more recent Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation	No change	Lourenco 2008
Length of stay: MonopolarTURP (LOS_MTURP)	3.03	3.03 Source: Original NICE Guidance (EAC report p75). Same LOS was used in the more recent Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation	No change	Weighted average of HRG4 codes LB25A, LB25B, LB25C (HSCIC 2013)

Length of stay: Urolift (LOS_PUL)	0.5	0.125 This LOS was agreed and used in the final base case for the Urolift NICE guidance (MTG26; pages 11 and 92). This length of stay (routinely 3 hours) has been confirmed in numerous reports from NHS hospitals. This LOS was also used by the EAC for the day case scenario in the recent Urolift guidance review (p11 of 15)	No change	Used for day case scenario. All routes are day patient or clinic in
Length of stay: Rezum (LOS _Rezum)		0.5 Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation	0.5 [Alternative would be 0.125]	Rezum submission was based on equivalence to Urolift. Therefore scenario modelled using 0.125, same value as Urolift.
Theatre time (minutes)				
bipolar TURP (theatretime_BTURP)	55.44	66 Source: Original NICE Guidance (EAC report p75). Same procedure time was used in the more recent Rezum Medical Technology Guidance 2020 (MTG49), Supporting	55.44	In MTG26 the EAC updated mTURP to 66 minutes, but BiTURP was unchanged at 55.44 minutes

		Documentation (p126-127)		
HoLEP (theatretime_HOLEP)	79.96	80.2 Source: Original NICE Guidance (EAC report p75). Same procedure time was used in the more recent Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation (p126-127)	79.96	This is the value stated in EAC assessment report p75, and used in the model. There will be minimal difference in the result.
monopolar TURP (theatretime_MTURP)	66	66 Source: Original NICE Guidance (EAC report p75). Same procedure time was used in the more recent Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation (p126-127)	No change	
Urolift procedure (theatretime_PUL)	30 30 minutes in submitted model, EAC calculated weighted average of 60 minutes	14 Source: [redacted]	No change	Accept change of practice and new data. Note that MTG49 Rezum used 30 min based on clinical advice.
Rezum procedure (theatretime_Rezum)	Not included in original model	17.5	No change	

		Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation		

Company base case results

Table 6: Economic model results for the original Urolift guidance and for the guidance update (using data submitted by the company and the EAC's amendments)

Scenario	Original guidance			Submitted update (2020)			EAC base case (2020)	
	Per patient cost	Incremental cost vs. Urolift		Per patient cost	Incremental cost vs. Urolift		Per patient cost	Incremental cost vs. Urolift
Urolift – Outpatient	n/a	n/a		£2,240	£ -		£2,250	£ -
Urolift – day case	£2,405	£ -		£2,265	£24		£2,275	£24
Urolift - inpatient	£2,979	£574		n/a	n/a		n/a	n/a
Rezum	n/a	n/a		£2,306	£66		£2,297	£47
BiTURP	£2,564	£159		£3,297	£1,057		£3,166	£915
MonoTURP	£2,691	£286		£3,388	£1,148		£3,415	£1,164
HoLEP	£2,315	-£90		£3,543	£1,303		£3,428	£1,178

Results

The EAC's amended cost model reports that the base case for Urolift as an outpatient procedure is cost-saving compared to the included comparators. The amount saved varies between the different comparators:

- Urolift is cost saving by £47 per patient compared with Rezum
- Urolift is cost saving by £915 per patient compared with BiTURP
- Urolift is cost saving by £1,164 per patient compared with MonoTURP
- Urolift is cost saving by £1,178 per patient compared with HoLEP

Sensitivity analysis

One-way sensitivity analysis

The company provided one-way sensitivity analysis for the number and price of Urolift devices, the number of additional devices required for median lobe treatment, the proportion of treatments for median lobe and the incidence of UTI with Rezum.

The company also completed probabilistic sensitivity analysis showing that Urolift with no anaesthetist was the cheapest option in 59.4% of 10,000 model iterations.

The EAC repeated the company's sensitivity analysis with the updated EAC base case.

Table 7 One-way sensitivity and threshold results

Variable changed	Range	Threshold		Description
		company	EAC	
Number of Urolift implants	3-6	3.65	3.61	Rezum is cheaper option if over threshold
Price of Urolift implants	350 – 425	£417.55	£412.65	Rezum is cheaper if Urolift cost is over threshold. [redacted]

Additional implants for treating median lobe	0-3	-	-	Urolift remains cheaper
Probability of hyperplasia being present in the median lobe	0.02-0.2	0.178	0.143	Rezum is cheaper if probability is greater than threshold
Incidence of urinary tract infection after Rezum treatment	0.02-0.17	-	-	Urolift remains cheaper The company submission states that the cost of Rezum treatment increases to £2,421 at 17%, which is the upper range from Mollengarden 2018
Theatre time Urolift	10 - 30	NA	16.70	Urolift cost saving if LOS < threshold
Length of stay: Rezum	0.1-0.5	NA	0.374	Rezum cost saving if LOS < threshold
Length of stay: Urolift	0.1-0.5	NA	0.248	Urolift cost saving if LOS > threshold
Cost of follow up consultation, Urolift	15.7 - 110	NA	£87.09	Urolift cost saving if followup > threshold. This is less than cost for other procedures.
Length of stay: BiTURP	0.5-2.63	NA	-	Urolift remains cost saving, although BiTURP approaches values for Rezum and Urolift when LOS BITURP=0.5 days
Theatre time Rezum	0-17.5	NA	15.17	Urolift is cost saving

Additional Scenarios presented by EAC

The EAC calculated scenarios for the following scenarios, shown in table 8.

Table 8 Impact of EAC Scenarios

Scenario	Impact
Length of stay for Rezum is 0.125 days	Urolift no longer cost saving compared to Rezum
All follow-ups by telephone consultation, for all comparators	Reduction in costs for all comparators, Urolift no longer cost saving compared to Rezum
BiTURP has day surgery, using Length of stay =0.5 days	Reduction in costs for all technologies except HoLEP, Urolift remains cost saving compared to all.
Remove staff costs from theatres – there is an element of double counting in the costs used.	Reduction in costs for all technologies. Urolift remains cost saving compared to all.
Alternative increased costs for UTI	Minor difference. Urolift remains cost saving compared to all.

1% for Rezum and Urolift for incontinence, based on MTG49 assumption	Increased cost for Urolift and Rezum, Urolift remains cost saving compared to all.
Theatre time for Urolift is 30 min, based on previous guidance (MTG26)	Urolift no longer cost saving compared to Rezum

The length of theatre time for Urolift in the cost model for this guidance update on Urolift is 14 minutes. The cost model in the original Urolift guidance used a theatre duration of 30 minutes. The EAC's sensitivity analysis notes that Urolift is cost saving compared to Rezum, if theatre time is less than 16.7 minutes.

In order to explore the evidence for theatre time for Urolift, the EAC prepared the following table (table 9) to show the length of stay and theatre time reported in the included studies. The EAC notes that none of the studies gave a clear definition for procedure time and there is likely to be a difference between theatre time and anesthesia time as shown in Bardoli et al (2017).

Table 9 Length of stay and procedure time for Urolift

Study	Setting	N Urolift	Length of stay (days)	Procedure time (minutes)
Roehrborm et al (2015) L.I.F.T study	USA Canada Australia	140	0.19	66.16 procedure time.
Sonksen (2015) The BPH6 study.	Denmark UK Germany Italy	45	1	55 minutes Anaesthesia time
Bozkurt (2016)	Turkey	17	<1 day	29.1 minutes operation time.
Gratzke et al (2016) The BPH6 study.	Germany UK Denmark	45	Not reported	Not reported
Rukstalis et al (2016) L.I.F.T study	USA Canada Australia	51	0.21 days	51.25 Anaesthesia time
Bardoli et al (2017)	UK	11	10.6 hours (0.44 days)	8.5 minutes operation time. 18.7 minutes theatre time
Roehrborm et al (2017) L.I.F.T study			Not reported	Not reported
Eure et al (2019)	USA	1413	Not reported	Not reported

	Australia			
Sievert et al (2019)	Germany	86	2.0 days	57 minutes operation time
Rubio et al (2019)	Spain	20	4.5 hours (0.1875 days)	12 minutes operative time.
Tutrone and Schiff (2020)	USA	53	Not reported	Not reported
NHS Norfolk and Norwich (2019)	UK	322	3-4 hours (0.125 – 0.167 days)	25 minutes
NHs Northampton	UK	20	0,27 days	20.11 minutes operating time
NHS Frimley Park	UK	75	Day case	25 minutes
NHS St Helens and Knowsley Teaching Hospital	UK		Day case	10-30 minutes (excluding 35 minutes induction and recovery time)
NHS Fife	UK	42	Not reported	17 minutes
NHs Royal Devon and Exeter	UK	93	Not reported	Not reported

Comparison with cost model in original Urolift guidance (MTG26)

The EAC noted that the cost model submitted for the guidance update reported lower costs for Urolift treatment than in the original guidance (MTG26, 2015). The key elements of this cost reduction were from:

- Reducing the number of implants per surgery, from 4 to 3.5 (reduction of £200, based on submitted audit data). The EAC notes that in most of the included studies 4 or more implants are used.
- Reducing time in theatre from 30 minutes to 14 minutes (reduction of £322.24, based on submitted audit data)
- Changing the follow-up for Urolift surgery to a telephone consultation (reduction of £72.33 – using EAC values of £37 for patient facing nurse time)

The company's submission for the guidance update also included increased costs for BiTURP, MonoTURP and HoLEP compared to the original guidance (MTG26, 2015). The key elements of this cost increase, in addition to inflation, come from:

- Increase in consumables costs for biTURP, and to a lesser extent for o monoTURP.

- Increased impact of incontinence due to change in calculations between models.

In the model for MTG26 guidance, the incontinence rates were applied only to patients where treatment had failed. In the current submitted model the incontinence rates are applied to the whole population who have treatment

Comparison with cost model used in Rezum guidance (MTG49)

The model can also be compared to that submitted for MTG49 Rezum (2020), in which Rezum was cost saving compared to Urolift. Both models took many variables and model structure from both MTG26 Urolift and MTG29 Greenlight.

The key changes in the current submitted model for Urolift, compared to MTG49 are:

- Reduced change in theatre time for Urolift from 30 to 14 minutes (included studies are between 8min and 1 hour, 4 are closer to an hour)
- Reduced length of stay for Urolift from 0.5 days to 0.125 days.
- Change to telephone consultation for Urolift.
- Additional trial without catheter (TWOC) appointment for Rezum (this was included in some EAC scenarios for MTG49)

MTG49 guidance accepted a value of 0.5 days for both Urolift and Rezum for the length of stay. This was based on the value of 0.5 days for one of the scenarios in MTG26, and an assumption that the length of stay for Rezum would be equal to Urolift. In the current model, length of stay for Rezum remains at 0.5 days, but for Urolift it has been reduced to 0.125 days to reflect the accepted guidance for day case surgery. If both were set at 0.125, Rezum would be cost saving compared to Urolift.

EAC conclusions on the economic evidence

The EAC updated the costs in the economic model submitted by the company. This caused a small reduction in cost savings for Urolift leading the

EAC to conclude that day-case Urolift surgery is roughly cost neutral (saving £47 per patient) compared to Rezum. This cost neutral position relies upon:

- a reduction in the number of Urolift implants used and in the length of theatre time. The evidence to support this reduction in number of implants comes from [redacted] This reduction is also supported by local audits carried out in NHS Trusts and from NICE shared learning documents (NHS Fife 2020; [redacted]; [redacted]; Royal Devon & Exeter NHS Trust 2020; Norfolk & Norwich NHS Trust 2019).

- The length of stay is 0.5 days for Rezum (as per the cost model in MTG49) and is 0.125 days for Urolift. MTG49 included the assumption that Urolift and Rezum both have the same length of stay, but if this scenario is added to the de novo cost model for the Urolift guidance update, then Urolift is no longer cost saving (whether both have 0.5 or 0.125 days' stay).

- Urolift has a telephone follow-up consultation with a nurse whereas other procedures have an outpatients follow-up appointment with a consultant. If telephone follow-up consultations are used for all comparators then Rezum becomes cost-saving compared with Urolift. The company stated that telephone follow-up would not be possible for Rezum as patients are discharged with a catheter in situ and would need to attend an in-clinic trial without catheter appointment.

The EAC concluded that Urolift is cost saving compared to mono TURPS, biTURPS or HoLEP in the EAC base case and in the scenarios explored by the company and the EAC. Urolift is either cost-saving or cost-neutral compared to Rezum in the EAC base case, however this is dependent on several assumptions. The majority of the scenarios exploring these assumptions result in Rezum becoming cost-saving compared with Urolift in either of the branches of the cost model.

5 Ongoing research

One relevant clinical trial was identified via clinicaltrials.gov.uk:

- NCT04338776 – Comparing UroLift experience against Rezum. Not yet recruiting.

Six other relevant trials were identified but had either finished recruitment or had withdrawn.

6 Issues for consideration by the Committee

Clinical evidence

- The clinical evidence for Urolift is of moderate to high quality. It suggests that that Urolift improves BPH symptoms over time, but that the magnitude of improvement is lower than those seen for TURP in symptom severity and urological outcomes. However, UroLift does appear to be superior to Rezum for erectile dysfunction and symptom severity outcomes.

- Rukstalis et al; 2018 have not been discussed in full as the comparator is outside of scope. However, reported that UroLift is as beneficial for people with obstructing median lobe as for people with lateral lobe obstruction, in relation to symptom severity, ejaculatory and erectile dysfunction, urological and quality of life measures.

- The EAC concluded that the studies included in this guidance update show a similar pattern of results over time, in that Urolift results in improvements in symptom severity measures, urological outcomes and quality of life measures

Cost evidence

- The EAC's conclusion of the economic evidence was that Urolift is either cost-saving or cost neutral compared to Rezum in the EAC base case, however this is dependent on several assumptions. They regarded that the majority of the scenarios exploring these assumptions result in Rezum becoming cost-saving compared with Urolift.

- Key assumptions in the economic model are reductions in the number of Urolift implants used, length of theatre time, the difference in length of stay for Urolift (0.125 days) and Rezum (0.5 days) and the use of telephone follow-up consultation with a nurse for people having Urolift while other procedures have an outpatients follow-up appointment with a consultant.

Equalities considerations

The company identified three areas related to equality for consideration:

- The prevalence of LUTS secondary to BPH increases with advancing age. Advanced age is an independent predictor of adverse outcomes after all surgery, including for BPH.

- People of non-white family origin have been shown be at higher risk of adverse outcomes following BPH surgery.

- UroLift is classed as a low-risk procedure and is associated with a lower risk of complications compared to standard resection procedures

- Teleflex is aware of 8 patients who identify as female who have had UroLift.

7 Authors

Harriet Unsworth, Senior HTA analyst

Chris Pomfrett, Technical adviser – research commissioning

NICE Medical Technologies Evaluation Programme

September 2020

Appendix A: Sources of evidence considered in the preparation of the overview

A Details of assessment report:

- Dr Laura Knight, Dr Helen Morgan, Megan Dale, Cedar, Cardiff and Vale UHB; MT241 UroLift Assessment Report Update; September 2020

B Submissions from the following sponsors:

- Teleflex

C Related NICE guidance

- UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia. NICE Medical technology guidance MTG26 (2015). Available from https://www.nice.org.uk/guidance/mtg26
- Rezum for treating lower urinary tract symptoms secondary to benign prostatic hyperplasia. NICE Medical technology guidance MTG49 (2020). Available from https://www.nice.org.uk/guidance/mtg49
- Insertion of prostatic urethral lift implants to treat lower urinary tract symptoms secondary to benign prostatic hyperplasia. NICE interventional procedure guidance IPG 475 (2014). Available from www.nice.org.uk/guidance/IPG475
- Lower urinary tract symptoms in men: management. NICE clinical guideline CG97 Last updated June 2015. Available from www.nice.org.uk/guidance/CG97

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Appendix B: Comments from professional bodies

Expert advice was sought from experts who have been nominated or ratified by their Specialist Society, Royal College or Professional Body. The advice received is their individual opinion and does not represent the view of the society.

Ian Pearce

Consultant Urological Surgeon, British Association of Urological Surgeons

Tamer El-Husseiny

Consultant Urological Surgeon, GMC, BMA, European Association of Urology, Endourological Society

Maya Harris

Consultant Urologist, BAUS, AUA, EAU, Royal College of Surgeons of England

Raj Persad

Consultant Urologist, St Joseph's Hospital NHS Trust

Nitin Shrotri

Consultant Urologist, East Kent Hospitals University NHS Foundation Trust.

Nikesh Thiruchelvam

Consultant Urologist, Cambridge University Hospitals NHS Trust

Rajesh Kavia

Consultant Urological Surgeon, London North West University Healthcare NHS Trust

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Consultant Urologist, Kingston Hospital NHS Foundation Trust

Mark Rochester

Consultant Surgeon, Norfolk and Norwich University Hospital NHS Foundation Trust

Vinnie During

Consultant Urological Surgeon New Cross Hospital, Wolverhampton

James Andrew Thomas

Consultant Urological Surgeon, Princess of Wales Hospital

Francis Keely

Consultant Urologist, Bristol Urological Institute

Tom McNicholas

Consultant Urological Surgeon, Past President, Royal Society of Medicine, Section of Urology, Pinehill Hospital, Hitchin; Spire Hospital, Harpenden

Karen McCutcheon

Director of Education, School of Nursing and Midwifery, Queen's University Belfast, Medical Biology Centre

- The experts generally regarded Urolift to be an effective and innovative treatment for BPH.
- They noted that Urolift could be offered to people who were medically unfit and others who were classed as high risk for surgical options that require anaesthesia.
- Urolift could be particularly of benefit to younger men who wished to preserve sexual and ejaculatory function.

- The experts noted that other devices were available that were similar to Urolift, such as Rezum, but that these had different modes of action to Urolift.
- In general, the experts found the Urolift system to be reliable and easy to use.
- 2 experts noted that mis-firing of the delivery system, caused by user error, resulted in implants being wasted. 2 experts noted cases where implants had failed or complications had arisen from an implant.
- 4 experts noted that there is currently no long-term effectiveness for Urolift.
- 3 experts highlighted that Urolift implants cause an artifact to be seen on MRI scans and it is important for patients to be made aware of this.
- 8 experts noted that Urolift presented costs savings compared to other treatment options because it could be delivered as a day-case surgery. 2 considered that cost comparisons against non-surgical treatment options would be beneficial.

Appendix C: Comments from patient organisations

Advice and information from patient and carer organisations was not sought for this guidance update.

Appendix E: decision problem from scope

Population	Men with lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) aged 45 or over, and with prostate volumes no greater than 100 ml
Intervention	The UroLift system in inpatient or day case setting
Comparator(s)	•Monopolar or bipolar transurethral resection of the prostate (TURP) •Holmium laser enucleation of the prostate (HoLEP) •Transurethral water vapour therapy using Rezum (NxThera Inc)
Outcomes	The outcome measures to consider include: •Length of hospital stay •The need for, or duration of, post-operative catheterisation •Number of post discharge follow-on consultations, both in primary and secondary care settings •Time to re-operation and re-operation rates •Symptoms of BPH (using the International Prostate Symptom Score [IPSS]) •Changes in ejaculatory or sexual function •Time to return to normal activities •Quality of life •Hospital-acquired infection •Theatre and staff time •Incidence of chronic atonic bladder, detrusor sphincter dyssynergia, chronic urinary infection, chronic renal failure •Device-related adverse events •Number of implants
Cost analysis	Comparator(s): Monopolar or bipolar TURP, HoLEP and Rezum Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be long enough to reflect differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers of implants and combinations of devices are needed.
Subgroups to be considered	Men for whom TURP or HoLEP is unsuitable because of operative risk including risks of blood loss or anaesthesia.
Special considerations, including those	Men who wish to preserve sexual function and fertility.

related to equality		
Special considerations, specifically related to equality	Are there any people with a protected characteristic for whom this device has a particularly disadvantageous impact or for whom this device will have a disproportionate impact on daily living, compared with people without that protected characteristic?	No
	Are there any changes that need to be considered in the scope to eliminate unlawful discrimination and to promote equality?	No
	Is there anything specific that needs to be done now to ensure the Medical Technologies Advisory Committee will have relevant information to consider equality issues when developing guidance?	No
Any other special considerations	Not applicable	

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology guidance scope

UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia (Guidance update)

1 Technology

1.1 Description of the technology

The UroLift system (NeoTract) is used to perform a prostatic urethral lift, a procedure that is an alternative to current standard surgical interventions such as transurethral resection of the prostate (TURP) and holmium laser enucleation (HoLEP). The UroLift system uses adjustable, permanent implants to pull excess prostatic tissue away so that it does not narrow or block the urethra. In this way, the device is designed to relieve symptoms of urinary outflow obstruction without cutting or removing tissue.

The UroLift system comprises 2 single-use components: a delivery device and an implant. The delivery device consists of a hand-held pistol grip to which a needle-shaped probe is attached. Each UroLift implant consists of a superelastic nitinol capsular tab, a polyethylene terephthalate monofilament, and a stainless steel urethral end-piece. The surgeon inserts the probe into the urethra until it reaches the prostatic urethra (the widest part of the urethral canal); a fine needle at the end of the probe deploys and secures an implant in a lobe of the prostate. One end of the implant is anchored in the urethra and the other is attached to the firm outer surface of the prostatic capsule, so pulling the prostatic lobe away from the urethra. This is repeated on the other lobe of the prostate. Typically about 4 implants are used. The procedure can

be done with the patient under local or general anaesthetic and may be done either on an in-patient or day-case basis.

1.2 Relevant diseases and conditions

Urolift is intended for use for the treatment of symptoms due to urinary outflow obstruction secondary to benign prostatic hyperplasia (BPH), including lateral and median lobe hyperplasia [2020], in men 45 years of age or older. It should not be used for men who have a prostate volume of more than 100 ml, or those who have a urinary tract infection, urethral conditions that prevent the insertion of the delivery system into the bladder, urinary incontinence due to incompetent sphincter, or current gross haematuria. The company states that UroLift can be performed under local anaesthetic, without an anaesthetist present, with light sedation if needed [2020].

The prevalence of BPH increases with age. The first pathological signs of BPH are seen in men aged 31-40, although prevalence is typically only 8%. This rate increases rapidly with age: around 60% of men aged 60 or older will experience some degree of prostate enlargement (NHS Choices), and over 80% of men aged 70 or older (Woo, 2012). BPH is the most common cause of lower urinary tract symptoms (LUTS), although the two are not necessarily synonymous.

The effect of LUTS on quality of life can be assessed using the International Prostate Symptoms Score (IPSS). A score of 8-19 is classified as moderate, while 20-35 is classified as severe. Moderate-to-severe LUTS are present in about 40% of men older than 50 years of age, rising to 90% of men in their eighties (Patient UK). Moderate to severe LUTS are estimated to affect up to 3.4 million men in the UK (Rees, 2014), and up to 15,000 men undergo TURP annually in England and Wales to relieve symptoms (NHS Direct Wales).

1.3 Current management

NICE CG97 Lower urinary tract symptoms in men: management (2010) recommended surgical interventions for men with BPH only when LUTS are severe or drug treatment and conservative management have been

unsuccessful or are not appropriate. If symptoms worsen over time, or if conservative management or drug treatment options are inappropriate or unsuccessful, surgical options may be considered.

For voiding LUTS, options include monopolar or bipolar TURP, transurethral vaporisation of the prostate (TUVP) or holmium laser enucleation of the prostate (HoLEP). Transurethral incision of the prostate (TUIP) may be offered if the prostate is estimated to be smaller than 30 g. Open prostatectomy should only be offered if the prostate is estimated to be larger than 80 g.

These treatments may be unsuitable for some people, due to the size and width of the prostate, size of the median lobe or position of the bladder neck. If the prostate is too large for transurethral surgical interventions, an open prostatectomy may be offered. All surgical comparators (except TUIP) functionally reduce prostate tissue volume by destroying tissue and debulking the prostate, to relieve LUTS.

Minimally invasive treatments such as transurethral needle ablation (TUNA), transurethral microwave thermotherapy (TUMT), high-intensity focused ultrasound (HIFU), transurethral ethanol ablation of the prostate (TEAP) and laser coagulation are not recommended by NICE for people with lower urinary tract obstructive symptoms (NICE guideline lower urinary tract symptoms in men: management). The clinical guideline recommends offering adjustable prostatic implants (such as the UroLift system) for the treatment of storage symptoms only as part of a randomised controlled trial. Insertion of prostatic urethral lift implants to treat lower urinary tract symptoms secondary to benign prostatic hyperplasia (NICE interventional procedure guidance 475) concluded that there is adequate evidence on the safety and efficacy of the procedure to support its use, provided that clinicians have specific training in the insertion of the implants.

1.4 Regulatory status

The UroLift system received a CE mark in November 2009 as a prostatic retraction implant for use in treating urinary outflow obstruction secondary to benign prostatic hyperplasia. The instructions for use specify that it is indicated for use in men aged 50 years and older and is contraindicated in men that have prostates larger than 100 ml.

1.5 Claimed benefits

The benefits to patients claimed by the company are:

- Reduction in diminished ejaculatory or sexual function
- Reduced need for post-operative catheterisation and reduced catheterisation time
- A quicker return to pre-treatment activities following treatment
- Reduced risk of hospital-acquired infection as the UroLift system is a day procedure, which does not require inpatient hospitalisation.

The benefits to the healthcare system claimed by the company are:

- Reduction in hospital length of stay, since UroLift is conducted as a day procedure
- Reduction in inpatient resource use, such as theatre operating time and associated staffing costs and resources.
- Significantly lower number of post discharge follow-on visits, both in primary care settings and in an outpatient setting, saving physician resources
- Reduced adverse event profile, leading to savings associated with the cost of complications associated with other surgical procedures
- Reduced costs from the avoidance of conditions brought on by treatment neglect such as atonic bladder, chronic kidney infection or failure, or detrusor sphincter dyssynergia, from the use of UroLift system in men who would not otherwise consider surgical treatment

2 Decision problem

Population	Men with lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) aged 45 or over, and with prostate volumes no greater than 100 ml
Intervention	The UroLift system in inpatient or day case setting
Comparator(s)	•Monopolar or bipolar transurethral resection of the prostate (TURP) •Holmium laser enucleation of the prostate (HoLEP) •Transurethral water vapour therapy using Rezum (NxThera Inc)
Outcomes	The outcome measures to consider include: •Length of hospital stay •The need for, or duration of, post-operative catheterisation •Number of post discharge follow-on consultations, both in primary and secondary care settings •Time to re-operation and re-operation rates •Symptoms of BPH (using the International Prostate Symptom Score [IPSS]) •Changes in ejaculatory or sexual function •Time to return to normal activities •Quality of life •Hospital-acquired infection •Theatre and staff time •Incidence of chronic atonic bladder, detrusor sphincter dyssynergia, chronic urinary infection, chronic renal failure •Device-related adverse events •Number of implants
Cost analysis	Comparator(s): Monopolar or bipolar TURP, HoLEP and Rezum Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be long enough to reflect differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers of implants and combinations of devices are needed.
Subgroups to be considered	Men for whom TURP or HoLEP is unsuitable because of operative risk including risks of blood loss or anaesthesia.
Special considerations, including those related to equality	Men who wish to preserve sexual function and fertility.

Special considerations, specifically related to equality	Are there any people with a protected characteristic for whom this device has a particularly disadvantageous impact or for whom this device will have a disproportionate impact on daily living, compared with people without that protected characteristic?	No
	Are there any changes that need to be considered in the scope to eliminate unlawful discrimination and to promote equality?	No
	Is there anything specific that needs to be done now to ensure the Medical Technologies Advisory Committee will have relevant information to consider equality issues when developing guidance?	No
Any other special considerations	Not applicable	

3 Related NICE guidance

Published

- Northampton General Day Case BPH service evaluation – adoption of Urolift. Shared learning, January 2020. Available here: https://www.nice.org.uk/sharedlearning/northampton-general-day-case-bph-service-evaluation
- Lower urinary tract symptoms in men. NICE pathway, last updated April 2020. Available from: https://pathways.nice.org.uk/pathways/lower-urinary-tract-symptoms-in-men
- Prostatic urethral temporary implant insertion for lower urinary tract symptoms caused by benign prostatic hyperplasia. NICE interventional procedures guidance IPG641. January 2019. Available here: https://www.nice.org.uk/guidance/IPG641
- Urolift – a community-based alternative treatment for Benign Prostatic Obstruction (BPO). Shared learning, November 2019. Available from: https://www.nice.org.uk/sharedlearning/urolift-a-community-based-alternative-treatment-for-benign-prostatic-obstruction-bpo
- Prostate artery embolisation for lower urinary tract symptoms caused by benign prostatic hyperplasia. NICE interventional procedure guidance,

IPG611, April 2018. Available from: https://www.nice.org.uk/guidance/ipg611

- Transurethral water jet ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia, NICE interventional procedures guidance IPG629, September 2018. Available from: https://www.nice.org.uk/guidance/ipg629
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- Adoption of UroLift procedure, an ambulatory pathway for patients suffering from Lower Urinary Tract Symptoms of Benign Prostatic Hyperplasia. Shared learning, November 2016. Available from: https://www.nice.org.uk/sharedlearning/adoption-of-urolift-procedure-an-ambulatory-pathway-for-patients-suffering-from-lower-urinary-tract-symptoms-of-benign-prostatic-hyperplasia
- Insights from the NHS: adoption of UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia at St Helens and Knowsley Teaching Hospital NHS Trust. NICE shared learning, September 2016. Available from: https://www.nice.org.uk/sharedlearning/insights-from-the-nhs-adoption-of-urolift-for-treating-lower-urinary-tract-symptoms-of-benign-prostatic-hyperplasia-at-st-helens-and-knowsley-teaching-hospital-nhs-trust
- Insights from the NHS: adoption of UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia at Frimley Park Hospital. NICE shared learning, August 2016. Available from: https://www.nice.org.uk/sharedlearning/insights-from-the-nhs-adoption-of-

urolift-for-treating-lower-urinary-tract-symptoms-of-benign-prostatic-hyperplasia-at-frimley-park-hospital

- GreenLight XPS for treating benign prostatic hyperplasia. NICE medical technologies guidance MTG29, June 2016. Available from: https://www.nice.org.uk/guidance/mtg29
- Insertion of prostatic urethral lift implants to treat lower urinary tract symptoms secondary to benign prostatic hyperplasia. NICE interventional procedure guidance, IPG475, January 2014. Available from: http://guidance.nice.org.uk/IPG475
- Lower urinary tract symptoms in men. NICE quality standards, QS45, September 2013. Available from: http://publications.nice.org.uk/lower-urinary-tract-symptoms-in-men-qs45#
- Lower urinary tract symptoms secondary to benign prostatic hyperplasia: tadalafil. NICE Evidence summary: new medicine, ESNM18. Available from: http://www.nice.org.uk/mpc/evidencesummariesnewmedicines/ESNM18.jsp
- Prostate Artery embolisation for Benign Prostatic Hyperplasia. NICE interventional procedure guidance, IPG453, April 2013. Available from: http://guidance.nice.org.uk/IPG453
- Lower urinary tract symptoms: Evidence Update March 2012. A summary of selected new evidence relevant to NICE clinical guideline 97 'The management of lower urinary tract symptoms in men' (2010). Available from: https://www.evidence.nhs.uk/about-evidence-services/bulletins-and-alerts/evidence-updates
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- The management of lower urinary tract symptoms in men. NICE clinical guideline, CG97, May 2010. Available from: http://www.nice.org.uk/cg97
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- Holmium laser prostatectomy. NICE interventional procedure guidance, IPG17, November 2003. Available from: http://www.nice.org.uk/guidance/IPG17
- Transurethral electrovaporisation of the prostate. NICE interventional procedure guidance, IPG14, October 2003. Available from: http://www.nice.org.uk/guidance/IPG14

In development

NICE is developing the following guidance:

- Rezum for treating lower urinary tract symptoms secondary to benign prostatic hyperplasia. NICE medical technology guidance. Expected publication date 24th June 2020.
- Guidance update to MTG23: The PLASMA system for transurethral resection of the prostate. (The PLASMA system was formerly known as TURis). NICE medical technology guidance update. Publication date to be confirmed.

4 External organisations

4.1 Professional

The following organisations have been asked to comment on the draft scope:

- British Association of Day Surgery
- The Association for Perioperative Practice
- British Association of Urological Surgeons
- British Prostate Group
- The College of Operating Department Practitioners
- Royal College of Anaesthetists
- Royal College of Surgeons of England

4.2 Patient

NICE's Public Involvement Programme contacted the following organisations for patient commentary and asked them to comment on the draft scope:

- Bladder and Bowel Foundation
- Bladder and Bowel UK
- Everyman
- Men's Health Forum (MHF)
- Orchid (for penile, prostate and testicular cancer)
- Prostate Help Association
- Tackle Prostate Cancer

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Health Technology Evaluation

Review decision

Review of MTG26: UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia

This guidance was issued in September 2015.

NICE proposes an update of published guidance if the evidence base or clinical environment has changed to an extent that is likely to have a material effect on the recommendations in the existing guidance. Other factors such as the introduction of new technologies relevant to the guidance topic, or newer versions of technologies included in the guidance, will be considered relevant in the review process, but will not in individual cases always be sufficient cause to update existing guidance.

1. Review decision

Update the guidance to allow the MTAC committee to consider changes in the estimated costs and clinical considerations for using UroLift in day case procedures and in people with obstructing middle lobes.

A list of the options for consideration, and the consequences of each option is provided in Appendix 1 at the end of this paper.

2. Original objective of guidance

To assess the case for adoption of the use of UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia.

3. Current guidance

1.1 The clinical case for adopting the UroLift system for treating lower urinary tract symptoms of benign prostatic hyperplasia is supported by the evidence. The UroLift system relieves lower urinary tract symptoms while avoiding the risk to sexual function associated with transurethral resection of the prostate (TURP) and holmium laser enucleation of the prostate (HoLEP). Using the system reduces the length of a person's stay in hospital. It can also be used in a day-surgery unit.

1.2 The UroLift system should be considered as an alternative to current surgical procedures for use in a day-case setting in men with lower urinary tract symptoms of benign prostatic hyperplasia who are aged 50 years and older and who have a prostate of less than 100 ml without an obstructing middle lobe.

1.3 The primary cost drivers in the model were the cost of each implant and the number of implants used per treatment (the modelling assumed 4). Compared with

monopolar and bipolar transurethral resection of the prostate (done as an inpatient procedure, which is most common), using the UroLift system in a day-surgery unit results in cost savings of around £286 and £159 per patient. There was uncertainty over the procedure duration in the model, but this made little difference to the cost case.

4. Rationale

There is no functional change to the technology and no change to the care pathway since MTG26 was published.

There is new clinical evidence. Although the new clinical evidence supports the clinical conclusions from the original guidance for UroLift, there has been a change to the price of UroLift. The updated cost modelling showed that the UroLift system is likely to be cost saving only when compared with monopolar TURP in day surgery scenarios, with a reduction in cost saving from £286 per patient at the time of original guidance to £28 per patient, and an additional saving of £100 when purchasing UroLift in a box of 10 implants. UroLift is no longer cost saving when compared with bipolar TURP unless the implant is purchased in bulk and the procedure is done without an anaesthetist in the day surgery scenario. The clinical experts advised that a consultant anaesthetist would usually be present when the UroLift system was used in a day-surgery scenario. Therefore, to follow the MTEP process guide, the recommendation is to let MTAC consider a standard update to the guidance to reflect the change in estimated costs to the NHS based on current prices and new assumptions with regard to clinical contexts.

5. New evidence

The search strategy from the original assessment report was re-run. References from Jan 2015 onwards were reviewed. Additional searches of clinical trials registries were also carried out and relevant guidance from NICE and other professional bodies was reviewed to determine whether there have been any changes to the care pathways. The company was asked to submit all new literature references relevant to their technology along with updated costs and details of any changes to the technology itself or the CE marked indication for use for their technology. The results of new evidence are presented in the 5.4 section below. See Appendix 2 for further details of ongoing and unpublished studies.

5.1 Technology availability and changes

The technology is still available to the NHS. Since the guidance was published in September 2015, no change has been made to the technology.

The price for UroLift has increased from £330 to [redacted].

5.2 Clinical practice

The NICE pathway is lower urinary tract symptoms in men. The clinical pathway is unchanged in terms of diagnosis and therapeutic options. Since the publication of MTG26 UroLift, MTEP have produced MTG29 Greenlight that is an alternative therapy for the same population and considered by the same pathway. NICE QS45 Lower urinary tract symptoms in men gives criteria for assessing the efficacy of clinical procedures that may be applied to any surgical intervention.

The NICE guideline on lower urinary tract symptoms in men: management recommended surgical interventions for men with BPH only when LUTS are severe or drug treatment and conservative management have been unsuccessful or are not appropriate, but the guideline does not make specific recommendations on named technologies. Minimally invasive treatments such as transurethral needle ablation (TUNA), transurethral microwave thermotherapy (TUMT), high-intensity focused ultrasound (HIFU), transurethral ethanol ablation of the prostate (TEAP) and laser coagulation are not recommended by NICE for people with lower urinary tract obstructive symptoms.

Since the publication of MTG26, the technology has added a new indication, and the use of UroLift has expanded to people with obstructing middle lobes. Evidence from a prospective, non-randomised US study evaluating the safety and effectiveness of the prostatic urethral lift (PUL) in 45 men with middle and median lobe characteristics (Rustalis et al. 2018), suggested that men with BPH including those with middle lobe obstruction, can be treated with the PUL procedure safely and effectively. Expert advice was received from 9 consultant urologists who use the technology in their practice and 1 senior registrar who has not used UroLift but had training. Most experts were not aware of any significant changes to the clinical pathway since the guidance was published, and 3 experts indicated a competing technology (Rezum) has been introduced in the NHS. Some experts are aware that new evidence is available (medlift study) on using PUL for obstructive median lobes since MTG26 was published. One expert carried out the UroLift procedure on people with median lobes. Expert advice was that the technology is specifically beneficial for those who are unfit for major surgery, and younger patients (e.g. aged under 65 years) who wish to preserve their sexual function. All experts considered special training such as simulation training is needed to use the technology safely.

5.3 NICE facilitated research

None.

5.4 New studies

Results from the NICE literature search as well as information from the company and clinical experts were used to assess new relevant evidence. A total of 10

publications on 7 individual studies were identified as being relevant to this guidance review, all of which are comparative studies. The new studies included information on lower urinary tract symptoms, urinary flow rate, quality of life, sexual function and device-related adverse events. One retrospective before and after comparison study was conducted in the NHS setting (Bardoli et al. 2017). Details on the study design, population and key results of each study are summarised below:

Randomised controlled trials

Luminal Improvement Following prostatic Tissue (LIFT) study

Roehrborn et al. (2015b) is a study of 3-year results of the LIFT trial. Over 3 years follow up, 129 (92.1%) men receiving PUL completed the follow-up. Of these 129, 93 were included in the analysis, and 36 were not included due to missing data (n=3), protocol deviation (n=3), the use of medication at time of follow-up (n=13), unrelated PUL procedures (n=2), and surgical retreatment (additional PUL=6; TURP or laser vaporisation=9). Results indicated that both voiding and storage function improve significantly by 4 weeks after PUL and this improvement remained in 3-year follow up (n=93, IPSS change[1]= 41.1% reduction, 95% CI 48.2% to 34.6% reduction). At 3 years quality of life (QoL) and peak flow rate (Qmax) remained significant improvement by 48.8% and 53.1% respectively. Participants underwent prostatic urethral lift (PUL) procedure had average erectile function measured by sexual health inventory for men score above baseline at all follow-up time points. Ejaculatory function was improved in the 3-year follow-up (8.9%, p=0.0129). Male Sexual Health Questionnaire for Ejaculatory Dysfunction (MSHQD-EjD) bother associated with ejaculatory function was also improved significantly at every follow-up point (p≤0.0002).

Roehrborn et al. (2017) is a study of 5-year results of the LIFT trial. Results showed that there was a moderate decrease in IPSS improvement over 5 years. Results indicated that sustained improvement in urinary symptoms (n=72, IPSS, 35.9% reduction, 95% CI 44.4 to 27.3% reduction; quality of life, -50.3%, 95% CI -58.4 to -42.2%; n=71, BPHII, 51.8%, 95% CI -63.2 to -40.5%), and urinary flow rate (n=52, Qmax, 44.3%, 95% CI 29.4 to 59.1%). At 5 years 19 patients were re-treated including 18 had severe baseline LUTS (IPSS 20 or more). There was no significant degradation in mean erectile function (n=49, IIEF-5, 6.1%, 95% CI -12.9 to 25.2%) or ejaculatory function (n=49, MSHQ-EjD function, 9.3%, 95% CI -3.8 to 22.5%) over the course of 5 years. MSHQD-EjD bother due to ejaculatory function improved and remained significantly improved at 5 years (n=49, -6.3%, 95% CI -31.5 to 18.8%, p=0.0195). Over the 5-year study follow-up, few related adverse events occurred

[1] The reduction indicates the improvement in symptoms.

after the initial 3 months, with a total of 1 adverse event reported between 49 and 60 months.

Rukstalis et al. (2016) is a study of 2-year results of 53 men with moderate-to-severe LUTS who had underwent a blinded sham procedure in the LIFT trial. Of 66 patients undergoing sham procedure in the LIFT study, 53 (80%) elected to have PUL treatment after the LIFT primary endpoint comparison at 3 months, and 51 were included the analysis. Both the IPSS and Qmax showed significant and durable improvement through 24 months, with the IPSS reduced by 9.6 points which was equivalent to 35.5% improvement (n=42, p<0.001) and Qmax increased by 4.2mL/second (equivalent to 77.2% improvement; n=36, p<0.001) compared with baseline (at the time after randomisation). Quality of life including IPSS QoL and BPHII improved significantly after the PUL procedure and maintained the improvement over 24 months. The sexual function questionnaire-based average measures showed significant improvements after PUL (MSHQ-EjD function, n=31, improved by 40.6%, p<0.001; MSHQ-EjD bother, n=31, improved by 50.0%, p=0.001). Of 241 devices implanted into the 53 men, 10 devices were later found to have been misplaced. Over the 24-month follow-up period, 3 patents had their encrusted devices removed, and one additional patient underwent removal of a non-encrusted device prophylactically. In each case LUTS either remained stable or improved after removal.

BPH 6 study

Sonksen et al. (2015) is a prospective randomised non-inferior trial. Patients were from 3 European countries, and were randomly assigned to receiving PUL or TURP and compared LUTS improvement, recovery, worsening of erectile and ejaculatory function, continence and safety (BPH 6[2]) over 12-months follow-up. A total of 91 patients enrolled and 80 underwent assigned treatment (TURP=35; PUL=45). There were differences in baseline parameters between 2 treatment groups except the MSHQ-EjD function score.

- Significant improvements in IPSS, IPSS QoL, BPH II, and Qmax were observed in both PUL and TURP groups at 12 months, and patient underwent TURP had greater improvement in symptoms (IPSS: TURP n=32, -15.4 points versus PUL n=41, -11.4 points; p=0.02) and Qmax (TURP, n=30, 13.7 points versus PUL n=32, 4.0 points, p<0.0001) compared with those had PUL.

[2] A reduction of 30% more in IPSS at 12 month; QoR VAS 70% or more by 1 month; Reduction of <6 points for SHIM during 12 months; response to MSHQ-EjD question 3 indicating emission of semen during 12 month; incontinence severity points (ISI) 4 points or less at all follow-up; No treatment related adverse event greater than grade 1 on the Clavien-Dindo classification at any time during the procedure or follow-up.

- PUL patients had more rapid recovery than TURP patients over 3.5 months follow-up with significantly more PUL patients reporting 70% or more quality of recovery but the difference between two groups were not significant are the end of study follow-up (12 months).

- Erectile function was preserved in both PUL and TURP groups as measured by SHIM scores, and majority of men had a reduction of 6 points or less during 12 months and no significant difference between 2 groups.

- Patients in the PUL group experienced an improvement in average ejaculatory score (MSHQEjD) from baseline to the end of study follow-up, but the TURP group had a significant decline.

Gratzke et al. (2017) is a study of 2-year results of the BPH 6 trial on 80 patients. Significant improvements in IPSS, IPSS QoL, BPH Impact Index (BPHII) and Qmax were observed in both PUL and TURP arms through 2-year follow-up. IPSS change with TURP was superior to that with PUL at 1 and 2 years, and TURP was superior with regard to Qmax over 2 years follow-up. Ejaculatory function was superior for PUL compared with TURP ($p < 0.001$), with patients in the TURP arm experiencing a significant decline ($p < 0.001$) in MSHQ-EjD function score from 1 month after the procedure and onwards. Both treatments achieved a clinically important improvement in health related QoL.

Before and after comparison studies

Bozkurt et al. (2016) is a retrospective, non-randomised study evaluating the change in symptoms, urinary function, quality of life and sexual function in 17 men who underwent PUL due to an indication of BPH in Turkey. Significant differences were observed in the mean IPSS, UFM, PVR and QoL scores but there was no significant change in terms of the IIEF and MSHQ-EjD over the 12 months follow-up.

Bardoli et al. (2017) is a retrospective, non-randomised UK study evaluating the impact of UroLift on urinary symptoms, function and quality of life in 11 men who were suitable for the procedure. Results reported a statistically significant reduction of 36% in the IPSS score at 4 months post-operatively (mean IPSS score 25.4 [SD=5.5] at baseline versus 16.3 [SD=9.4], p=0.02). Quality of life showed a 1.6 points reduction (p=0.04) at 4-month follow-up. There was an average increase in flow rate to 8.9ml/s but change in Qmax was not statistically significant (p=0.39).

Rustalis et al. (2018) is a prospective, non-randomised US study evaluating the safety and effectiveness of the PUL in 45 men with middle and median lobe characteristics. Participants were followed for 1 year and assessed on symptom response (IPSS), quality of life (QoL and BPHII), Qmax, sexual function (IIEF, and MSHQ-EjD) and adverse events. Results indicated that the mean IPSS improvement at 1, 3, 6, and 12 months was at least 13.5 points and significantly better than

baseline at every time point. QoL and BPHII were improved significantly (>60% and >70%, respectively at 3, 6, and 12 months) compared with the baseline. Mean Qmax had significant improvement ranged from 90–130% throughout follow up. There was no significant degradation in mean erectile function (IIEF-5) over the course of follow up. At 1-year follow-up, surgical retreatment for failure to cure occurred in 1 man (2%) who received additional PUL implants at 9 months with no adverse effect from the presence of implants.

Sievert et al. (2018) is a prospective, non-randomised German study examining the outcome of PUL in 86 men who underwent the PUL procedure in 24 months follow-up. General anaesthesia was used in 64 patients and local anaesthesia was used in 24. Of the 86 patients, 74 (86%) reported substantial symptom relief with significant decreases in mean IPSS from 20.82(SD=6.5) at baseline to 10.2 (SD=3.9) at the end of study follow-up (p<0.0001). They also reported quality of life improvement with a significant decrease in quality of life score from baseline of 4.1 (SD=1.2) to 2.0 (SD=3.9) at the month 24 (p<0.0001). Significant functional improvement was also seen, with a decrease in mean PVR from 150 ml at baseline to 51 ml (6 months) and 45 ml (24 months), and an increase in mean Qmax from 11.1 ml/s to a peak at 1 month of 15.5 ml/s (p=0.005) and leveling to 14.2 ml/s at 24 months (p=0.005). Eleven patients (12.8%) needed retreatment due to persistence of LUTS or had remaining increased PVR, including 9 having TURP, 1 undergoing PUL and 1 not having any treatment.

Real world versus trial evidence

Eure et al. (2019) is a retrospective US study evaluating the effectiveness and safety of PUL using data collected in a real-world setting. A total of 1,413 people who underwent PUL were included: 1,248 spontaneously voiding patient and 165 patients with urinary retention. Compared with the L.I.F.T. study, study participants were older (67 versus 70 years, p<0.001) had lower baseline IPSS (22.3 versus 19.2, p<0.0001) and QoL (4.6 versus 4.0, p<0.0001) but higher Qmax (7.9 versus 12.6mL/second, p<0.0001). After PUL, IPSS improved significantly from baseline at all timepoints including 12 months (n=241, -8.1 point, equivalent to 39% decrease, p<0.0001) and 24 months (n=151, -8.3 point, equivalent to 37% decrease, p<0.0001). For subjects with baseline IPSS≥13, IPSS improvement and percentage change at 1, 3,6,12 and 24 months were not significantly different compared with people from the L.I.F.T. study. QoL also improved significantly from baseline at 12 and 24 months follow-up, by 39% (n=190) and 41% (n=118) reduction respectively. Changes in Qmax were not significant from baseline to 12 months (15% increase, p=0.7), and 24 months (32% increase, p=0.08) follow-up. Over the course of the study, 72 people underwent either a PUL retreatment (n=39) or an alternative surgical intervention (17 laser procedures and 16 TURPs), 11of which included removal of implants. Only one additional person required a procedure specifically to remove a UroLift System implant.

5.5 Cost update

The cost model from the original guidance was updated by the External Assessment Centre (EAC) which prepared the original assessment report (Cedar).

The original cost model was revised to incorporate:

- the updated technology prices
- updated NHS resource costs to current values

The company have submitted updated costs for both the capital cost and consumables used for UroLift (see Table 1). [redacted]. The company state that there is no change planned to this provision.

Table 1 Updated unit costs

The EAC analysed the evidence provided by the company and the clinical experts contacted for this guidance review and concluded that, given the clinical pathway has not changed since the initial assessment, the overarching model structure and assumptions remain valid. All costs have been updated to current prices. The EAC updated the base case and the scenario analysis, where UroLift procedures were carried out in day surgery with or without an anaesthetist.

Consumables for procedure	**2014 value**	**Updated 2019 costs**	**EAC Comments**
UroLift device (per implant)	£330.00	[redacted]	Cost submitted by company
Loop electrode (Monopolar TURP)	£52.50	£58.72	Inflated using PSSRU equipment index from 2009-10 to 2017-18
Loop electrode (Bipolar TURP)	£52.50	£58.72	
Morcellator blade (HoLEP)	£664.63	£743.37	
Fibre (HoLEP)	£614.37	£687.15	
Capital costs			
UroLift Capital cost	£5,199	[redacted]	Company submitted cost
TURP Capital cost (mono polar and bipolar)	£0	£0	Same assumption
HoLEP Capital cost	£167,555	£187,403.70	Inflated using PSSRU equipment index from 2009-10 to 2017-18
Other costs			
Consultant anaesthetist, per hour	£99.00	£108	PSSRU 2019, Table 14, Consultant: medical, per working hour

Tables 2 to 3 present the updated base case, showing the results in 2014 and the updated results using implant prices when purchased individually and in a box of 10. The UroLift system was cost incurring comparing with TURP and HoLEP.

Table 2 The updated the base case (the company submission)

			Implants cost £[redacted] each		**Implants cost £[redacted] in box of 10**	
	2014 Cost	**Cost compared with UroLift**	**2019 Cost**	**Cost compared with UroLift**	**2019 Cost**	**Cost compared with UroLift**
UroLift	£2,342	-	£2,781	-	£2,681	
Monopolar TURP	£2,339	-£3	£2,510	**-£271**	£2,510	**-£170.71**
Bipolar TURP	£2,302	-£41	£2,476	**-£305**	£2,476	**-£205.05**
HoLEP	£1,924	-£418	£2,074	**-£707**	£2,074	**-£606.94**

Table 3 the updated base case (EAC assessment report, incorporating changes made by the EAC)

			Implants cost £[redacted] each		**Implants cost £[redacted] in box of 10**	
	2014 Cost	**Cost compared with UroLift**	**2019 Cost**	**Cost compared with UroLift**	**2019 Cost**	**Cost compared with UroLift**
UroLift	£2,979	-	£3,484	-	£3,374	

Monopolar TURP	£2,707	-£272	£2,893	**-£591**	£2,893	**-£481.02**
Bipolar TURP	£2,579	-£400	£2,763	**-£721**	£2,763	**-£611.05**
HoLEP	£2,762	-£217	£2,976	**-£508**	£2,976	**-£397.81**

Table 4 and 5 present the results for scenario analyses, showing the updated costs when UroLift is carried out in day surgery with and without an anaesthetist. During the development of original guidance, the clinical experts advised that a consultant anaesthetist would usually be present when the UroLift system was used in a day-surgery scenario.

Table 4 The updated EAC scenario for day theatre, excluding anaesthetist.

			Implants cost £[redacted] each		**Implants cost £[redacted] in box of 10**	
	2014 Cost	**Cost compared with UroLift**	**2019 Cost**	**Cost compared with UroLift**	**2019 Cost**	**Cost compared with UroLift**
UroLift	£2,355	-	£2,795	-	£2,695	
Monopolar TURP	£2,691	+£336	£2,877	**+£82**	£2,877	**+£182**
Bipolar TURP	£2,564	+£209	£2,746	**-£48**	£2,746	**+£52**
HoLEP	£2,315	-£40	£2,485	**-£309**	£2,495	**-£209**

Table 5 The updated EAC scenario for day theatre, including anaesthetist time.

			Implants cost £[redacted] each		**Implants cost £[redacted] in box of 10**	
	2014 Cost	**Cost compared with UroLift**	**2019 Cost**	**Cost compared with UroLift**	**2019 Cost**	**Cost compared with UroLift**
UroLift	£2,405	-	£2,849	-	£2,749	
Monopolar TURP	£2,691	+£286	£2,877	**+£28**	£2,877	**+£128**
Bipolar TURP	£2,564	+£158	£2,746	**-£102**	£2,746	**-£2**
HoLEP	£2,315	-£90	£2,485	**-£363**	£2,485	**-£263**

6. Summary of new information and implications for review

The new clinical evidence supports the committee's clinical conclusions from the original guidance. The updated cost modelling shows that the UroLift system is only cost saving when compared with monopolar TURP in the day surgery scenario, and this cost saving has reduced from £286 in the original guidance to £28 per patient. UroLift is no longer cost saving when compared with bipolar TURP.

An update to the guidance is recommended to reflect the change in the estimated costs and to evaluate the current use of UroLift.

A search of US Food and Drug Administration's MAUDE database between 1st September 2015 and 30 September 2019 found 59 cases reported on UroLift, including excessive bleeding, injury, device malfunction and 1 death.

7. Implications for other guidance producing programmes

UroLift is one of the Accelerated Access Collaborative (AAC) rapid uptake products, and is supported by the Innovative Technology Payment (ITP).

There is an option within the MTEP process to update the guidance within another piece of NICE guidance. There is no existing technology appraisal guidance relevant

to UroLift, therefore this is not considered further. The NICE clinical guideline on lower urinary tract symptoms in men: management (CG97) was initially published in 2010 and updated in June 2015. NICE will update the guideline to reflect current clinical practice. The review of MTG26 has already started, and the update of the guidance could be completed before the clinical guideline update. If CG97 incorporates UroLift, it will be a class of technology and not a named technology, therefore it is considered appropriate to update the existing MTG guidance for this device.

NICE MTEP is currently developing the guidance for Rezum, a minimally invasive procedure for treating people with lower urinary tract symptoms secondary to benign prostatic hyperplasia. Experts noted that Rezum has been used in some NHS hospitals. The Rezum procedure involves water vapour therapy and has a similar indication to the UroLift system: for treating lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) in those aged 50 or over, and with prostate volumes no greater than 100 cc (100 g).

8. Implementation

The company have confirmed that over 100 NHS Trusts are currently providing the UroLift procedure. No update data on the UroLift procedure is available prior to April 2017 because a new OPCS code was introduced to identify this procedure as part of the Innovation and Technology Tariff. A search of hospital episode statistics data indicated 779 admissions for endoscopic insertion of prosthesis to compress lobe of prostate in 2017/18 including 605 day-case admissions and 602 admissions in people aged 60 years or over.

A NICE shared learning example describing the use of UroLift has been published (NICE, November 2016). One of the key learning points was “Surgeons may want to perform initial cases under a general anaesthetic until they are confident with the procedure. After this, the procedure can easily be performed under a local anaesthetic, or light sedation if required.”

9. Equality issues

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

No equality issues were raised in the original guidance.

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Appendix 1 – explanation of options

If the published Medical Technologies Guidance needs updating NICE must select one of the options in the table below:

Options	**Consequences**	**Selected – 'Yes/No'**
Amend the guidance and consult on the review proposal	The guidance is amended but the factual changes proposed have no material effect on the recommendations.	No
Amend the guidance and do not consult on the review proposal	The guidance is amended but the factual changes proposed have no material effect on the recommendations.	No
Standard update of the guidance	A standard update of the Medical Technologies Guidance will be planned into NICE's work programme.	Yes
Update of the guidance within another piece of NICE guidance	The guidance is updated according to the processes and timetable of that programme.	No

If the published Medical Technologies Guidance does not need updating NICE must select one of the options in the table below:

Options	**Consequences**	**Selected – 'Yes/No'**
Transfer the guidance to the 'static guidance list'	The guidance remains valid and is designated as static guidance. Literature searches are carried out every 5 years to check whether any of the Medical Technologies Guidance on the static list should be flagged for review.	No
Defer the decision to review the guidance	NICE will reconsider whether a review is necessary at the specified date.	No
Withdraw the guidance	The Medical Technologies Guidance is no longer valid and is withdrawn.	No

Appendix 2 – supporting information

Relevant Institute work

Published

NICE IPG 475 Insertion of prostatic urethral lift implants to treat lower urinary tract symptoms secondary to benign prostatic hyperplasia (2014). The recommendation was that normal arrangements should be in place for clinical governance, consent and audit.

CG97 Lower urinary tract symptoms in men: management. Last updated June 2015. An update is planned.

In progress

NICE Medical technology guidance Rezum for treating benign prostatic hyperplasia.

Registered and unpublished trials

Trial name and registration number	Details
Prostatic Urethral Lift in Subject With Acute Urinary Retention Trial NCT03194737	A multi-centre, prospective evaluation of PUL and retrospective review of invasive surgery as potential comparator. The study is intended to be conducted at up to 5 different centres in the United Kingdom. Subject follow-up visits are at post-procedure, 6 weeks, 3 months, 6 months and 12 months. Recruitment Status: not recruiting (last updated Feb 2019) Estimated study completion date: February 2020 Estimated enrolment: 50participants Location: UK Funder: NeoTract, Inc

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National Institute for Health and Care Excellence

Medical Technologies Evaluation Programme

Review of MTG26 UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia

Consultation Comments table

There were 10 consultation comments from 6 consultees including 2 NHS professionals, 1 manufacturer, 2 MTAC Committee Members and 1 industry representative. The comments are reproduced in full, arranged in the following groups:

- The presence of an anaesthetist in the UroLift procedure
- A new indication for UroLift (median lobe)
- Equality issues

Table 1

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
1	2	Appendix 1	Agree that, given the change in inputs to the economic model and the emergence of other competing minimally invasive technologies, a review of the MTG is appropriate.	Thank you for your comment.
2	5	4	not all patients undergoing Urolift procedure will be suitable for day case without the presence of an anesthetist although this may be feasible in a lot of patients. Data is needed to suggest what proportion of patients undergoing Urolift can do so without the presence of an anesthetist. This will help to calculate costs and viability comparing Urolift with other procedures.	Thank you for your comment. NICE are grateful for information regarding the presence of an anaesthetist in the UroLift procedure. Staffing cost, such as an anaesthetist, will be considered in the update of guidance.

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
3	6	4	We dispute the inclusion of this scenario in which an anaesthetist isn't present during a day case procedure as we do not believe this is reflective of current UK clinical practice. Additionally the clinical expert advised that a consultant anaesthetist would usually be present in a day surgery scenario therefore this is not relevant for inclusion.	Thank you for your comment. The presence of an anaesthetist will be considered in the update of guidance.
4	6	5.2	*"Since the publication of MTG26, the technology has added a new indication, and the use of UroLift has expanded to people with obstructing middle lobes."* We disagree with this new indication due to the low weight of evidence being a single non randomised study of 45 patients. To add a new indication for this technology a significantly greater body of evidence should be required.	Thank you for your comment. NICE considers new evidence relevant to the technology and the need for any change in the scope will be considered in the update of guidance and in the light of new evidence.
5	5	5.4	patients with small median lobe can effectively be treated by Urolift according to recent evidence. However, more than 4 implants may be necessary in these treatments. Cost effectiveness should be judged on the basis of number of implants used as it makes the procedure more expensive.	Thank you for your comment. NICE are grateful for information regarding the new indication for the technology. This information will be included in the update of guidance.
6	6	7	*"If CG97 incorporates UroLift, it will be a class of technology and not a named technology,"* Development of additional technologist and techniques support this statement and future proof CG97.	Thank you for your comment.

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
7	3	9	* UroLift is delivered minimally-invasively and can be done as a day case surgery, and considered by many as an option for selected patients who are unsuitable for TURP. This would seem to be good news for frail elderly men who had been known to have increased mortality and morbidity after TURP. * It is suggested that reasonable adjustments should be considered for vulnerable individuals such as frail elderly men who live alone, or who have mental health conditions, cognitive impairment and learning difficulties in the choice of anaesthesia and provision of additional support in terms of consent, explanation of information and possibly aftercare to the patients, their carers and families.	Thank you for your comment. Equality issues and special considerations, including those related to equality, will be considered in the update of guidance.
8	3	Real world versus trial evidence	It is to be pointed out that long term data beyond 5 years, for instance, for retreatment rate, are not known.	Thank you for your comment.
9	4	Entire	Teleflex (the sponsor) have read the MTEP consultation on the review proposal for MTG26 (UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia). Teleflex will await the Standard Update before making further comment.	Thank you for your comment.
10	1	General	My worry with URolift as with other minimally invasive technologies which have been shown to provide benefit, is the unfounded criticism received from clinicians who do not use the	Thank you for your comment. Equality issues and special considerations, including those related to equality of access, will be considered in the update of guidance where relevant.

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			technique or who know little about it. Whilst the sensible approach is to accept 'one size does not fit all' and that selection criteria are all important in BPH treatment, there are tradiitionists who only do TURP who 'rubbish' other interventions like URolift with disredard to the data and disregard for patients wishes. I have had a number of patients denied appropriate intervention locally who have self -referred to me because of this intransigence to accept other techniques. Many of these patients have travelled long distances to my regret. Can we somehow avoid this obstruction to equity of access for patients?	

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Information request from the sponsor for Medical Technologies Guidance Update of MTG26 UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia

Update of MTG26 UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia

The original guidance was issued in September 2015.

The review decision for this guidance was issued in December 2019.

Contents

1. Company update

1.1 Changes in the technology

a) Is the technology still available to the NHS in the UK?

Yes

b) If the technology has changed, what it the latest current version and when was this model first marketed in the UK? Please provide technical specifications which show the differences.

No change to the technology

c) Does the new model perform the same function and use the same mode of action as the technology in MTG26?

N/A

d) Does the new model have a new CE mark?

N/A

e) Has the cost of the technology changed since the original guidance? Please give details (this can be kept commercial-in-confidence).

The current price of the Urolift implants is [redacted] (ex VAT) per implant. This information is provided as COMMERCIAL IN CONFIDENCE for the purpose of the Guidance Update process, however, the company acknowledge that the price will need to be included in the published updated guidance and give permission for this.

2. New evidence:

Is the company aware of any new clinical evidence on the use of UroLift, available since the original evaluation and Guidance Review (i.e. after March 2019)?

2.1 Published evidence - Urolift

(full copies are included in the accompanying submission pack)

a) Poster presented at BAUS 2019. Early results of Prostatic Urethral Lift (PUL) in subjects with Acute Urinary Retention (AUR). [Rochester M et al 2019]

Relevance to Guidance Update: The early results of this study show that Urolift can safely and quickly restore normal voiding in AUR patients with a history of BPH/LUTS while preserving erectile function. The 12-month follow-up of this study is available in an unpublished

abstract submitted for 2020 publication (please see Rochester *et al* in the Unpublished Evidence section below)

b) NICE Shared learning case study. Urolift – A community-based alternative for benign prostatic obstruction (BPO). Royal Devon & Exeter NHS Trust https://www.nice.org.uk/sharedlearning/urolift-a-community-based-alternative-treatment-for-benign-prostatic-obstruction-bpo [Royal Devon & Exeter NHS Trust 2020]

Relevance to Guidance Update: A real-world NHS case study showing how the adoption of Urolift enables the treatment of patients with obstructive LUTS in a community day case unit away from the main hospital, which frees up capacity for more urgent work such as cancer treatment. Also avoids issues associated with cancellations of lists or individual patients due to lack of availability of in-patient beds or prioritisation of more urgent cases in main theatres. Showed how adopting Urolift was able to significantly reduce the waiting list burden.

c) NICE Shared learning case study. Northampton General day-case BPH service evaluation. Northampton NHS Trust https://www.nice.org.uk/sharedlearning/northampton-general-day-case-bph-service-evaluation [Northampton NHS Trust 2020]

Relevance to Guidance Update: A real-world NHS case study showing how an NHS Trust was able to use its own PLICS data to show cost savings with Urolift compared with TURP.

d) NICE Shared learning case study. Adoption of Urolift procedure – An ambulatory pathway for patients suffering from lower urinary tract symptoms of benign prostatic hyperplasia. Norfolk and Norwich NHS Trust https://www.nice.org.uk/sharedlearning/adoption-of-urolift-procedure-an-ambulatory-pathway-for-patients-suffering-from-lower-urinary-tract-symptoms-of-benign-prostatic-hyperplasia [Norfolk & Norwich NHS Trust 2019]

Relevance to Guidance Update: A real-world NHS case study from a single trust with a large cohort of patients treated with Urolift. This case study was first published in 2016 and the case study was included in the information submitted to NICE in 2019. Since then, the trust has re-audited the practice and an update to the published case study was added in June 2019. This update contains data on 250 patients: average number of implants, procedure duration, length of stay and anaesthesia.

e) Poster presented at World Congress of Endourology 2018. Transforming BPH surgical care to an ambulatory setting – what are the gains and losses? [Young et al 2018]

Relevance to Guidance Update: A real-world NHS case study showing how a large NHS Trust [Leeds Teaching Hospitals] was able

to use its own PLICS data to show cost and other resource savings with Urolift compared with TURP.

f) NICE Shared Learning Case Study. Treating Benign Prostatic Obstruction (BPO) with UroLift in an outpatient setting. NHS Fife. https://www.nice.org.uk/sharedlearning/treating-benign-prostatic-obstruction-bpo-with-urolift-in-an-outpatient-setting [NHS Fife 2020]

Relevance to Guidance Update: A real-world NHS case study showing how transitioning to a pure local anaesthetic protocol without an anaesthetist present can enable Urolift to be performed routinely in an outpatient setting

g) Tutrone RF and Schiff W. Early patient experience following treatment with the Urolift prostatic urethral lift and Rezum steam injection. [Tutrone and Schiff 2020]

Relevance to Guidance Update: This is the first study to directly compare the early postoperative patient experience of Urolift and Rezum. The study shows that preliminary data suggests that Urolift provides a superior patient experience with better sexual function, lower catheterisation rates, less daily interference, and higher patient satisfaction in the recovery period compared to Rezum.

2.2. Unpublished evidence – Academic in confidence

(full copies are included in the accompanying submission pack)

Abstract:

[redacted]

Relevance to Guidance Update:

[redacted]

Abstract: Prostatic Urethral Lift - Influence of advanced techniques on benign prostatic enlargement patient pathway.

[redacted]

Relevance to Guidance Update:

[redacted]

[redacted]

Abstract: Prostatic Urethral Lift - Outcomes with prostatic urethral lift in urinary retention patients.

[redacted]

Relevance to Guidance Update:

[redacted]

Abstract: NHS experience of using prostatic urethral lift under local anaesthetic to treat obstructive lower urinary tract symptoms.

[redacted]

Relevance to Guidance Update:

[redacted]

a) Abstract:

[redacted]

Relevance to Guidance Update:

[redacted]

3. Adoption and usage data

Is the company aware of any adoption or usage data (such as audit) from the NHS or elsewhere?

The company provides the following adoption and usage data:

a) Procedure numbers, by NHS Trust, 2019/20, submitted to NHSE/NHSI as part of AAC Rapid Uptake Products programme. Commercial in Confidence. Please see ***Appendix 1. Procedure Numbers by NHS Trust***

[redacted]

b) [redacted]. Provides data on number of implants and procedure duration (example tracker template from NICE adoption support: https://www.nice.org.uk/guidance/mtg26/resources/urolift-case-data-tracker-a-realworld-example-whiston-hospital-excel-556235390 Commercial in Confidence. **Please see Appendix 2. Urolift patient tracker data**

[redacted]

4. List of NHS users

A list of NHS hospitals/users that provide an established Urolift service is provided with this submission Commercial in Confidence. We have also indicated within this list those NHS users who are doing Urolift lists under a local anaesthetic only (without sedation) and also those users who are transforming their service to an outpatient setting. Where known, we have indicated which NHS users are offering both Urolift and Rezum so have experience of both technologies. **Please see Appendix 3. NHS hospitals/users**

5. New indications

Has the technology added new indications or is now used in new applications not covered by the original guidance?

a. NHS pathway transformation to local anaesthetic only and outpatient/ambulatory setting

UroLift is routinely performed as a day case procedure under a local anaesthetic with occasional light sedation. Evidence for this is supported by the internal audit of NHS hospitals in which Urolift is being offered routinely to patients as a treatment option alongside the current standard of care. The British Association of Day Case Surgery (BADS) will be including Urolift in the next edition of 5th edition of the *BADS Directory of recommended Day and Short stay surgical procedures.*

More and more trusts have either transitioned or are looking to transition to a local anaesthetic only protocol, removing the need for an anaesthetist and paving the way to transition to an outpatient/ambulatory setting. Pathway Transformation Funding from the AAC was awarded to three trusts in 2019 to support this transition to an outpatient setting. This pathway transformation is expected to accelerate post-COVID-19, with greater emphasis on the need for:

- reducing aerosol-generating procedures, which have greater demand on PPE requirements
- reducing face-to-face contact time with hospital staff and the time patients spend in hospital
- reducing risk of readmission due complications
- reduce need for post-operative catheterisation

Evidence for this pathway transformation is provided in the unpublished evidence and audit data published in the NICE shared learning case studies.

The new outpatient (without anaesthetist) scenario is modelled in the accompanying cost model, alongside the current day case pathway.

b. Middle lobe

UroLift can now be performed in men with an obstructing middle lobe. Clinical evidence for this is supported by Rukstalis et al 2018 [Rukstalis et al 2018] Patients with obstructing middle lobes are now being routinely offered Urolift in NHS hospitals.

c. Acute urinary retention

Clinical study and empirical evidence from NHS trusts demonstrates that Urolift can be offered to men in acute and chronic urinary retention, safely and quickly restoring normal voiding without the risks associated with standard resective procedures.

Published evidence:

Poster. Rochester M et al. Early results of Prostatic Urethral Lift (PUL) in subjects with Acute Urinary Retention (AUR) [Rochester 2019]

Unpublished evidence:

[redacted]

6. Local anaesthesia protocol for Urolift

Example of local anaesthesia protocol employed in NHS hospitals

- Cold (4^{o}C), lidocaine gel 2%, 10 ml, instilled into the urethra, via syringe
- Clamp penis or patient holds glans for 10 minutes prior to the procedure
- Patient moved into theatre or outpatient procedure room, placed into Lithotomy position and draped

- Cold (4°C), Lidocaine gel 2%, 10 ml, instilled into the urethra, via syringe
- Scope and UroLift devices inserted while talking to patient
- If patient does not tolerate rigid cystoscopy on commencing procedure:
    - Protocol if anaesthetist present: Propofol / Fentanyl 2-10 ml, as required
    - Protocol if anaesthetist is not present: procedure is halted and patient is listed to have the procedure in theatre with sedation at a future date

Protocol verified by:

- Mr Petros Tsafrakidis, Consultant Urologist, NHS Fife*
- Mr Mark Rochester, Consultant Urologist, Norfolk and Norwich NHS Trust*

*Contact details provided in the NHS users. *Appendix 3*

7. Urolift – Reducing health inequalities and improving access

Urolift makes an important contribution to improving health inequalities in several protected characteristics:

- **Age:** The prevalence of lower urinary tract symptoms from BPH increases with advancing age. Many men who require surgical treatment for LUTS/BPH are often elderly. Advanced age has been shown to be an independent predictor of adverse outcomes after standard BPH surgery (TURP and laser) [Bhojani 2014]. As a minimally-invasive treatment, Urolift is associated with significantly lower risk of complications compared with standard resective procedures.

- **Gender reassignment**. Teleflex is aware of 8 patients worldwide who identify as women and who have undergone a Urolift procedure. One of these patients was an NHS patient. Details of the NHS clinician who undertook this procedure can be supplied on request and with the clinician's permission

- **Race**: Non-Caucasian race has been shown to be an independent predictor of adverse outcomes after standard BPH surgery (TURP and laser) [Bhojani 2014]. As a minimally-invasive treatment, Urolift is associated with significantly lower risk of complications compared with standard resective procedures.

Urolift enables greater access to treatment for LUTS/BPH:

- No requirement for general anaesthetic. Can be performed under a local anaesthetic. Particularly important in the context of high-risk patients who cannot undergo a general anaesthetic.
- No overnight stay requirement
- Minimal number of hospital visits required – reduced infection risk

- Rapid return to activities of normal living – particularly important for patients who, due to personal circumstances (eg carers) would find it difficult to undergo a procedure with an inpatient stay and long recovery time
- Sexual function: No de novo sustained erectile or ejaculatory dysfunction [Roehrborn 2017]. Particularly important for men who do not wish to risk losing sexual function with more invasive procedures such as TURP or laser.

Delays in treatment of BPH result in symptom progression and an increased risk of the patients presenting to A&E with UTI or acute urinary retention. Creating easier access to treatment through minimally-invasive treatment options, such as Urolift, will help to reduce risk of UTI and urinary retention that arise from delays to intervention.

8. Urolift – Supporting new ways of working following COVID-19 pandemic

Acute providers are facing significant challenges directly caused by the COVID-19 pandemic, especially dealing with a growing backlog of elective surgery, as well as the longer term service redesign that will be required to adapt to new ways of working. In the second phase of the response to COVID-19, NHS organisations are being asked to *'lock in' beneficial changes* that have been brought about in response to the virus. Providers are looking to transform services to reduce the time patients need to spend in hospital (either as an inpatient or simply the number of visits to hospital outpatients), reduce reliance on aerosol-generating procedures and move surgical procedures out of main theatres into the community or even into an outpatient / ambulatory setting.

Urolift helps to enable new ways of working and pathway transformation:

- Urolift can be performed under a local anaesthetic. More and more trusts have either transitioned or are looking to transition to a local anaesthetic only protocol, removing the need for an anaesthetist and paving the way to transition to an outpatient/ambulatory setting.
- Urolift is not an aerosol-generating procedures, which have greater demand on PPE requirements
- Urolift reduces the time that patients spend in hospital, the number of times that patients need to visit the hospital and the number of healthcare workers that patients come into contact with.
- Urolift is associated with a very low rate of post-operative complications [Roehrborn 2013], thereby reducing the risk of readmission
- Typically, most patients who have a Urolift procedure do not require catheterisation, therefore the requirement for the patient to return hospital for an appointment to remove the catheter is extremely low.

- As elective surgery begins again following the COVID-19 pandemic, treating patients with Urolift in settings away from the main theatre will help hospital trusts address their backlog of elective surgeries more quickly.

Evidence for this pathway transformation is provided in the published and unpublished evidence (see Section 2 for details).

The new outpatient (without anaesthetist) scenario is modelled in the accompanying cost model, alongside the current day case pathway.

8.1 Urolift: Impact on the care pathway

Transforming services with Urolift reduces the time that patients spend in hospital, the number of times that patients need to visit the hospital and the number of healthcare workers that patients come into contact with.

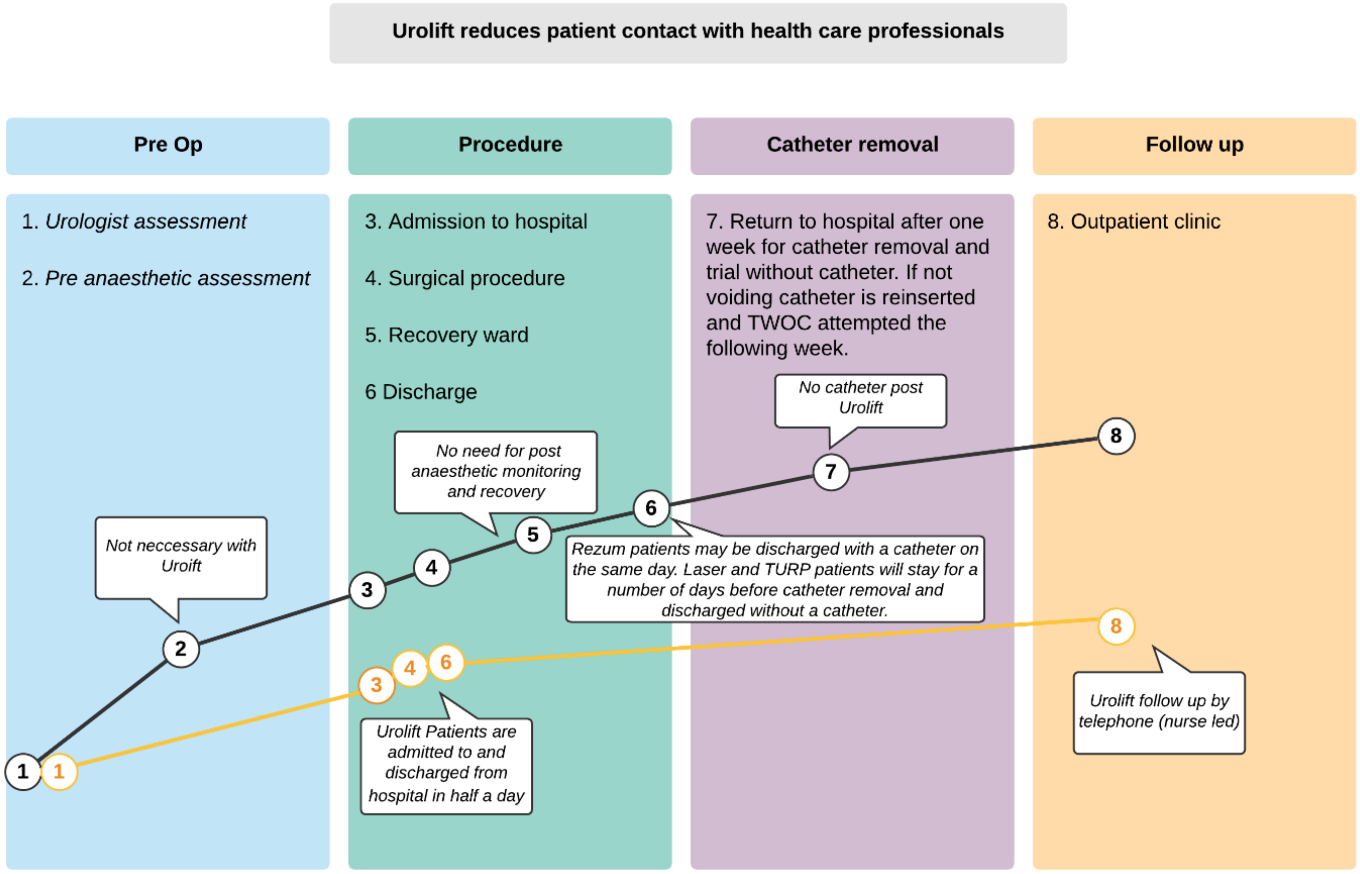
- **Pre-operative appointments:** Patients who have Urolift under a local anaesthetic without sedation do not need to attend an additional appointment for a pre-anaesthetic assessment. This is not the case for patients having other BPH procedures which require sedation.

- **Procedure**: Urolift can be performed in a procedure room with significantly fewer hospital staff present than in a theatre setting. Also, as Urolift can be performed under a local anaesthetic – patients are not intubated or extubated – so avoids aerosol-generating activity during the procedure. This is not the case for other BPH procedures that are performed under a general anaesthetic.

- **Recovery and discharge**: Patients who undergo general anaesthetic will take longer to recover and require monitoring. Rezum patients are typically discharged on the same day with a catheter in situ, while TURP and laser patients typically spend 1-2 nights in hospital and are discharged without a catheter once they are spontaneously voiding their bladder. In contrast, Urolift patients typically can be discharged from hospital immediately, and without a catheter in-situ, after spontaneous voiding of their bladder, on average an hour after their procedure. They can be discharged by nursing staff following a nurse-led discharge protocol, further reducing contact with health care professionals.

- **Catheter removal appointment**: Patients who are discharged with a catheter in-situ (all Rezum patients) will need to return to hospital after a few days to have the catheter removed and remain in hospital until they have voided urine. This outpatient appointment is called a ‘Trial without catheter’ and can last several hours. If the patient cannot void they will have a new catheter inserted and asked to return in another few days to attempt catheter removal again. Additionally, if a urinary infection occurs (up to 17% of Rezum patients [Mollengarden 2018], this may require additional contact or even readmission to hospital.

- **Follow-up:** Urolift patients do not have to return to hospital after the procedure and follow up can be performed over the telephone four weeks after the procedure. Patients being treated by any of the comparators will generally need to be followed up in a face-to-face appointment due to the invasive nature of the surgery.



9. Information provided in response to the change in scope

Following discussions within NICE it was decided to change the scope of the guidance update to include Rezum as a comparator. In every other respect the scope remains unchanged.

In this section, the company provides evidence and information to support evaluation of Urolift against the newly added comparator, Rezum.

NICE has published medical technologies guidance on Rezum (MTG49). At the time the Committee noted that there was no evidence that directly compares Rezum with other interventions for BPH, including Urolift.

Recently a study by Tutrone and Schiff has been published, which compare the early (up to 2 months following the procedure) patient experience of Urolift and

Rezum [Tutrone and Schiff 2020]. The authors concluded that the data suggests that Urolift provides a superior patient experience with better sexual function, lower catheterisation rates, less daily interference, and higher patient satisfaction in the recovery period compared to Rezum.

Comparisons of the efficacy and safety of Rezum with Urolift should be carefully scrutinised to ensure they can be fully supported by the evidence. In the development of the NICE guidance for Rezum [Rezum MTG49], the committee relied on comparisons of efficacy and safety there were based on comparing data from separate studies that are not analogous. It should be noted that the study populations between the Rezum II study and the LIFT study (Urolift) were different in the following critical aspects:

- The LIFT study excluded treatment of obstructing middle lobe (OML) [Roehrborn 2013]. McVary et al (Rezum II study) demonstrated that treatment of OML enhanced the overall IPSS and Qmax effect seen in this study [McVary et al., 2019]. In a recently published study with Urolift, looking at use in patients with OML, Rukstalis et al showed that treatment of OML shows a significantly greater effect on both IPSS (13.5 vs 10.6) and Qmax (6.4 vs 4.0 ml/s) [Rukstalis 2019]. The MedLift study was an FDA IDE extension of the LIFT randomised study, and was designed to examine safety and efficacy of Urolift for treatment of obstructive middle lobes (OML). Inclusion criteria were identical to the LIFT study, except for requiring an OML.

- Rukstalis et al went further in analysis to compute what the overall changes were in LIFT/MedLIFT studies if middle lobe was included [Rukstalis 2019]. The result (11.4 IPSS, 4.7ml/s Qmax) supports the lack of any significant chronic difference in effect between UroLift and Rezum.

- The Rezum II study, patient inclusion with regard to Qmax also biased results in favour of Rezum, when making outcome comparisons to the LIFT study. The Rezum II study excluded any patient with a baseline Qmax of less than 5 ml/s, whereas the LIFT study had no lower limit except complete retention. In LIFT, 26% patients were in this category of “near retention”, a patient population that, on average, has been shown to be less likely to have a quantitative improvement in Qmax [Guo 2017].

- In the Supporting Documentation to the Rezum NICE guidance [Rezum MT413], it was noted of the Rezum II study that the a*nalysis of the single-armed data was performed per protocol (PP) and attrition rates were significant, with 34% of patients not providing outcome data at 4 years [McVary et al., 2019].* The LIFT study, on the other hand showed 13.6% retreatment rate for Urolift at both 4 and 5 years with only 9% patients missing [Roehrborn 2017].

9.1 Comparing the mechanism of action of Urolift and Rezum

Rezum:

Rezum (Boston Scientific) is a tissue destructive thermal therapy for treating the lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH), similar to prior technologies using radiofrequency, microwave, and contact lasers as heat source. Rezum creates lesions in the enlarged prostatic tissue by destroying cells using steam injected into the prostate through a needle. This burns the tissue causing pain and discomfort to patients.

Because of the pain experienced by patients, the procedure can only be performed under general anaesthetic or by sedating patients using carefully administered lower doses of anaesthetic drugs, where it is hoped that intubation to support patients breathing can be avoided. The use of anaesthetic drugs in this way must be performed by an anaesthetist who will closely monitor the patient throughout the procedure and have full anaesthetic equipment ready should the patient require it.

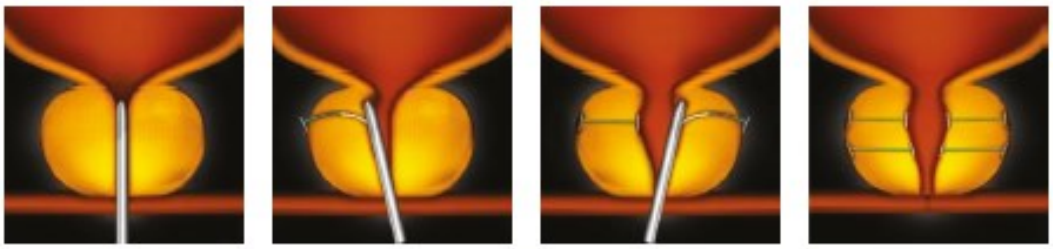
Once the steam burns the tissue and causes coagulative necrosis, an immediate inflammatory response is initiated in the same way that any body tissue responds to burning. This response causes swelling and oedema of the prostate tissue that further obstructs the urinary pathway, thus a urinary catheter must be placed in the bladder so that patients can safely pass urine. This catheter has to remain in situ until the inflammatory response reduces enough that patients can pass urine through the urethra. A catheter is in place on average about 5-7 days, but a catheter may be required for as long as 90 days in some patients. The combination of a potentially bacteria seeding catheter and necrotic prostatic tissue is likely the primary reason for a higher than normal infection rate, reported as high as 17% [Mollengarden 2018].

On average patients show some improvement by one month but many must endure the full healing process (typically several months), where necrotic tissue is resorbed, before significant improvement can be appreciated. If there is enough tissue reduction particularly in the obstructive aspects of the prostate at the end of this process, then the patients will feel an improvement in their LUTS

Urolift

The Urolift procedure involves small permanent implants, which are placed to retract the prostatic lateral lobes and reduce urethral obstruction without requiring disruption of prostate tissue. Because the periurethral tissue is compliant and the fibromuscular outer capsule is tough, applying this implant

under tension between the urethra and prostatic capsule lifts the urethra toward the capsule, expanding the urethral. In this way, Urolift immediately and permanently disobstructs the urethra without destroying or ablating prostate tissue. It is a mechanical mechanism that does not rely on surgical resection or ablation or a lengthy biologic process involving tissue necrosis. Unlike the other BPH procedures, the Urolift process is also reversable.



1. The UroLift® delivery device is placed through the urethra to access the enlarged prostate.

2. Each UroLift® delivery device retracts the obstructing prostatic lobes and deploys a needle that delivers a small, transprostatic permanent implant.

3. Every implant is assembled and tailored *in situ* as it is delivered.

4. The UroLift® delivery device is removed, leaving a more open urethra.

9.2 Comparison of Urolift and Rezum against key metrics of minimally invasive procedures to treat LUTS from BPH

Urolift is considered to be a minimally-invasive procedure compared with TURP or laser, the current standard of care for LUTS from BPH. Traditionally, the term minimally-invasive in the context of urology has tended to refer to endoscopic procedures vs open procedures. More recently, the term has been broadened to refer to procedures where the trauma to the body is minimised, thereby being associated with more rapid recovery, earlier discharge, reduced length of stay, less pain and complications.

The GIRFT Programme National Specialty Report for urology (2018) highlights the opportunities to deploy minimally invasive technology to increase the use of day surgery and perform treatments in an outpatients' setting [GIRFT 2018]. In particular, the report recommends the adoption of Urological Investigations Units (UIUs) which can provide *swift diagnosis and treatment without needing to admit patients*. Much of the work in a UIU can be led by specialist nurses rather than consultants, which releases consultant capacity to focus on more urgent work such as cancer.

Urolift does not resect or remove tissue. It is the only BPH procedure that does not do this and is therefore not associated with the common side effects and complications, such as bleeding and impact on sexual function that are associated with the resective procedures.

The following section provides a comparison of Urolift and Rezum against key metrics of minimally invasive urological procedures:

- Mechanism of action
- Anaesthesia
- Impact on sexual function
- Catheterisation
- Safety
- Procedure setting
- Procedure time
- Length of stay
- Patient selection
- Considerations for new ways of working – COVID-19
- Patient experience

It should be noted that only one study exists that directly compares Urolift and Rezum. This study was published very recently (June 2020) in the *Canadian Journal of Urology,*and compares the early patient experience of Urolift with Rezum [Tutrone and Schiff 2020].

Minimally invasive metric	Urolift	Rezum
Mechanism of action	Urolift uses specifically designed implants to mechanically retract the prostate tissue It does not involve tissue destruction, ablation or resection. Disobstruction of the prostate is immediate and permanent. The Urolift procedure is also reversible.	Rezum uses steam to thermally ablate prostate tissue by inducing tissue necrosis. Following the procedure, there is a gradual process of absorption, scarring and / or sloughing of necrotic tissue and the prostate shrinks, thereby disobstructing the urethra. Disobstruction is not immediate and takes several weeks.
Anaesthesia	UroLift is routinely performed as a day case procedure under a local anaesthetic with occasional light sedation. More and more trusts have either transitioned or are looking to transition to a local anaesthetic only protocol, removing the need for an anaesthetist and paving the way to transition to an outpatient/ambulatory setting. This move has been accelerated in some places to address the challenges presented by COVID-19. Evidence for where this approach has been adopted as standard of care is provided in the NICE Shared Learning case study from NHS Fife (provided in this submission in the *Published Evidence)*	In the recently published NICE guidance for Rezum (MTG49), it states that Rezum is usually done in the NHS under general anaesthesia or local anaesthesia with sedation. Clinical experts estimated that around two thirds of procedures done in the NHS are under general anaesthetic [MTG49].
Impact on sexual function	UroLift relieves lower urinary tract symptoms while avoiding the risk to sexual function associated with transurethral resection of the prostate (TURP) and holmium laser enucleation of the prostate (HoLEP) [NICE guidance MTG26]. This is a significant advantage for men who wish to preserve their sexual function.	Unlike Urolift which has been shown to preserve sexual function, Rezum is associated with a low risk of sexual dysfunction [NICE Guidance MTG49]

Catheterisation	In NHS and general UK clinical practice, Urolift typically does not need a post-operative urinary catheter.	After a Rezum procedure, a urinary catheter is left in place for 5 to 7 days to allow the dead prostate tissue to drain away [MTG49]. The impact of catheterisation and the risk of catheter-associated UTI is discussed in Section 9.3.
Safety	Compared with TURP and laser, Urolift has a very good safety profile. Most common adverse events reported include pain or burning with urination, blood in the urine, pelvic pain, urgent need to urinate, and the inability to control urine because of an urgent need to urinate. Most symptoms were mild to moderate in severity and resolved within two to four weeks after the procedure [Roehrborn 2013]	In the NICE guidance for Rezum, clinical experts advised that complications after the Rezum procedure are similar to those after other procedures for LUTS because of BPH and include urinary tract infections (UTIs), bleeding, epididymitis and abscess [MTG49]. The committee concluded that UTI is a common complication after Rezum [MTG49]. The need for catheterisation, combined with the presence of necrotic tissue, are considered by clinical experts to be predisposing factors for developing UTIs and, more rarely, urosepsis [MTG49]. This risk is higher for Rezum than UroLift, which usually does not need a post-operative urinary catheter [MTG49]. The clinical experts estimated that the risk of UTIs associated with a urinary catheter is around 5% to 7%, so a short course of prophylactic antibiotics may be prescribed after the procedure. Real-world clinical data suggests infection rates as high as 17% [Mollengarden 2018]
Procedure setting	Urolift can be done under a local anaesthetic without sedation. More and more trusts have either transitioned or are looking to transition to a local anaesthetic only	Rezum can be performed under local anaesthetic, but only when sedation is also given. This means

	protocol, removing the need for an anaesthetist and paving the way to transition to an outpatient/ambulatory setting. This move has been accelerated in some places to address the challenges presented by COVID-19. Evidence for performing Urolift in an NHS outpatient setting is provided in the NICE Shared Learning case study from NHS Fife (provided in this submission in the *Published Evidence).*	that moving the procedure out of theatre to an outpatient setting is impractical for most NHS trusts.
Procedure time	Procedure time for Urolift available from [redacted] (Appendix 2) indicate that the procedure is now being performed much faster than was conservatively estimated for the NICE Guidance developed in 2014. [redacted] indicates that the mean procedure time in NHS trusts over the past three years is 14 minutes (SD ±5 mins).	Procedure time for Rezum that was published in the NICE guidance (MTG49) is 20 mins.
Length of stay	Urolift patients are typically discharged after a few hours following the procedure. Average length of stay (LOS) for a Urolift procedure is 0.125 days. This LOS was used in the final base case for the Urolift NICE guidance (MTG26; pages 11 and 92 https://www.nice.org.uk/guidance/mtg26/documents/urolift-for-treating-lower-urinary-tract-symptoms-of-benign-prostatic-hyperplasia-assessment-report2). This length of stay (routinely 3 hours) has been confirmed in numerous reports from NHS hospitals. This LOS was also used by the EAC for the day case scenario in the recent Urolift guidance review (p11 of 15).	The average length of stay for Rezum is 0.5 days [MTG 49; Supporting documentation] The LOS is longer than for Urolift because of the sedation involved and the need to monitor patients following sedation.

Patient selection	Current NICE guidance for Urolift recommends it in patients who have a prostate of less than 100 ml without an obstructing middle lobe [MTG26]. New evidence presented in this guidance update extends its use to patients with obstructing middle lobes [Rukstalis 2019], and patients in AUR [Rochester 2019; Rochester 2020]. This means, with the exception of those with very large prostates (>100ml), Urolift can be offered to most patients for people with significant LUTS that have not responded to conservative therapy including medication and lifestyle changes.	The NICE guidance recommends Rezum in men with moderately enlarged prostate – typically between 30 cm3 and 80 cm3 [MTG49]. The guidance suggests that Rezum may not be suitable for everyone; Clinical experts said that Rezum should be avoided in people with prostatitis or confirmed prostate cancer, in people for whom day case treatment is impractical or unsafe, and if there's a risk of increased bleeding, for example if they're having anticoagulant treatment [MTG49].
Considerations for new ways of working – COVID-19	Urolift helps to enable new ways of working and pathway transformation following COVID-19: • Urolift can be performed under a local anaesthetic. More and more trusts have either transitioned or are looking to transition to a local anaesthetic only protocol, removing the need for an anaesthetist and paving the way to transition to an outpatient/ambulatory setting. • Urolift is not an aerosol-generating procedures, which have greater demand on PPE requirements • Urolift reduces the time that patients spend in hospital, the number of times that patients need to visit the	Rezum is more limited in the way it can enable new ways of working and pathway transformation following COVID-19: • Rezum cannot be performed under a local anaesthetic without sedation. This limits a transition of Rezum to an outpatient setting. • The NICE guidance for Rezum (MTG49) indicates that around two thirds of Rezum procedures done in the NHS are under general anaesthetic. General anaesthetic procedures are considered aerosol-generating, which have greater demand on PPE requirements • Rezum is performed under general anaesthetic or local anaesthetic with sedation. This means

	hospital and the number of healthcare workers that patients come into contact with.	patients are required to attend an additional outpatient appointment for a pre-op assessment. This increases the time that patients spend in hospital, compared with Urolift.
	• Urolift is associated with a very low rate of post-operative complications, thereby reducing the risk of readmission	• Rezum has a higher rate of post-operative complications compared with Urolift, thereby increasing the risk of readmission and requirement for further hospital appointments
	• Typically, patients who have a Urolift procedure do not require catheterisation, therefore the requirement for the patient to return hospital for an appointment to remove the catheter is extremely low.	• Rezum patients are discharged with a catheter in-situ. This means that they are required to return hospital for an appointment to remove the catheter.
Patient experience	Recently, a study by Tutrone and Schiff compared the early (up to 2 months following the procedure) patient experience of Urolift and Rezum [Tutrone and Schiff 2020]. *Recovery* During the 2 month period following the procedure, Rezum is associated with a higher level of interference from daily activity due to post-procedural voiding symptoms compared with Urolift. 42% of patients reported interference from entertainment related activities (eg cinema, theatre, spectator sports and cultural events) compared with 8% of Urolift patients (p=0.01). While 40% and 50% of Rezum patients (vs 12% and 0% of Urolift patients; p=0.04 and p=0.007) reported interference with community-related activities (eg volunteering, attending church, visiting family) and sport's related activities, respectively. *Satisfaction* • Significantly more Urolift patients (97%) rated their urinary symptoms as being at least "a little better compared with Rezum patients (70%); p=0.02. In contrast, More Rezum patients (22%) rated their symptoms were 'a little worse' or poorer compared with Urolift patients (3%); p=0.07. • Similarly, more Rezum patients (22%) reported being dissatisfied or very dissatisfied with their voiding symptoms, compared with Urolift patients (3%); p=0.07.	

	• Significantly more Rezum patients (26%) reported being dissatisfied or worse with their recovery compared with 7% of Urolift patients.

9.3 Implications for catheterisation following BPH procedures

Urolift is the only BPH procedure that does not typically require post-operative catheterisation. Patients treated with TURP or laser typically have a catheter for a few days, while patients treated with Rezum have a catheter for an average of 5-7 days [NICE guidance MTG49].

A urethral catheter is an indwelling flexible tube that is inserted through the urethra and then into the bladder in the aim of aiding a person to pass urine. Most urinary catheters in hospitals are inserted on a temporary basis to assist patient's recovery from surgery or acute illness. Patients may require a long-term catheter if they have an inability to pass urine without assistance. A common, and often serious complication from a catheter is a urinary tract infection (UTI) which if associated with a urinary catheter is called a catheter associated urinary tract infection (CAUTI). A urinary catheter significantly increases the risk of UTI and then possible severe complications such as sepsis [Letica-Kriegel et al 2019].

UTI is a leading cause of healthcare associated infection (HCAI) and gram-negative bloodstream infection (GNBSI) in England [Loveday et al 2014, Abernethy et al 2017 & Fitzpatrick et al 2016]. Numerous studies have highlighted that urinary catheters are associated with the majority of urinary HCAI and are the major risk factor for the incidence and severity of GNBSI [Melzer & Welch 2017 & Smith et al 2019].

In response to the continuing increase in the incidence of GNBSI, in 2016, the UK Government pledged to halve healthcare associated GNBSI by 2020 [DOH 2016]. Any strategy which reduces the incidence and duration of urethral catheterisation will reduce HCAI & GNBSI, improve patient outcomes and reduce additional financial burden from CAUTI complications.

Catheter Associated Urinary Tract Infection (CAUTI)

NICE (2019) define a CAUTI as:

> "Catheter-associated UTI is defined as the presence of symptoms or signs compatible with a UTI in people with a catheter with no other identified source of infection plus significant levels of bacteria in a catheter or a midstream urine specimen when the catheter has been removed within the previous 48 hours" [NICE 2019 www.pathways.nice.org.uk/pathways/urinary-tract-infections]

The longer a catheter is in place, the more likely bacteria will be found in the urine, and guidance from NICE states that catheters should be removed rather than changed, where possible [NICE 2019]. NICE (2014) states that urinary catheterisation should be used only after considering all alternative methods of management [NICE 2014].

Recent evidence suggests that between 34-54% of hospital CAUTI may be preventable, mainly due to the prevention of unnecessary catheterisation in the first place [Schreiber et al 2018]. Due to this, there are many NHS initiatives such as "*No*

Catheter NO CAUTI" which aims to reduce unnecessary insertions and promote catheter removal at the earliest opportunity when no longer clinically required. This initiative is being promoted by NHS England, NHS Improvement and the Academic Health Science Network (AHSN) with the focus on reducing unnecessary catheter use in the NHS https://improvement.nhs.uk/resources/urinary-catheter-tools https://www.ahsnnetwork.com/case-study/catheter-care-improvement-programme-brings-about-30-reduction-in-infection-rate

CAUTI and significance to catheter dwell time

The risk of developing a CAUTI is directly related to catheter dwell time. The longer the duration of catheterization, the more likely the risk of infection and complications [Clark et al 2019]. The EPIC 3 National evidence-based guidelines for preventing HCAI in NHS Hospitals in England [Loveday et al 2014] states that CAUTI risk increases significantly after 2 days of catheterisation. A large study (n=47,000) by Letica-Kriegal et al [Letica-Kriegal 2019] concluded that CAUTI increased with catheter duration; at 10 days 2.7% had CAUTI, 30 days 12% & 28.2% at 60 days.

The rate of development of catheter associated bacteriuria (presence of bacteria in urine) is approximately 3% to 7% per day [Clark et al 2019, Hooton et al 2010 & Lo et al 2014]. Bacteriuria is a risk factor for developing a CAUTI. Approximately 24% of bacteriuric patients will develop CAUTI, and of these, up to 4% develop a severe secondary infection [Clark et al 2019].

Following prostate surgery, evidence suggests there is an increased risk of CAUTI compared to non-urology surgery catheters [Li et al 2017]. This would be expected due to the localised trauma, inflammatory response and tissue necrosis at the surgical site compared to a patient who has not required surgery but has a catheter in situ.

NICE (2014) states that urinary catheterisation should be used only after considering all alternative methods of management.

Complications of CAUTI

The Centre for Disease Control (CDC) [CDC 2020] states: CAUTI can lead to such complications as prostatitis, epididymitis, and orchitis in males, and cystitis, pyelonephritis, gram-negative bacteremia, endocarditis, vertebral osteomyelitis, septic arthritis, endophthalmitis, and meningitis in patients. Complications associated with CAUTI cause discomfort to the patient, prolonged hospital stay, and increased cost and mortality. It has been estimated that each year, more than 13,000 deaths are associated with UTIs".
https://www.cdc.gov/nhsn/PDFs/pscManual/7pscCAUTIcurrent.pdf

CAUTI causes pain, discomfort and distress for patients. A catheter increases the likelihood of a CAUTI and studies have found that a catheter increases the incidence of acquiring severe sepsis (Melzer & Welch 2017). Duration of catheter of more than 3 days is associated with a significantly increased risk of sepsis [Schneidewind 2017]. Sepsis has a high chance of death and morbidity and has a large additional cost burden for the health care system.

Financial impact of CAUTI

The financial burden of CAUTI is considerable. Smith et al [Smith 2019] found that a CAUTI resulted in an increase length of hospital stay and direct hospital costs totalling over £263.8 million within England alone. They state that for every catheter prevented being inserted this would produce a cost saving per catheterisation of £142.

Psychological impact of catheterisation

A catheter has a psychological impact on patients, which may affect confidence and their psycho-social well-being. Catheter care education from a skilled urology professional is essential for a patient prior to be sending home with a catheter in situ. Studies have found that patients may have the following worries or concerns which impact on their lives with having a new catheter. These include familiarisation of catheter equipment, dealing with sexual activities, UTI, emptying of bags problems, catheter changes, clothing adjustments, positioning of tubing and kinking of catheter, pulling of catheter, odour, and worrying about catheter blocking or falling out. All of these have a significant impact on patients' quality of life and well-being [EAUN 2012].

Potential relevance of catheterisation when comparing Urolift with Rezum

In the NHS and the UK, typically patients treated with Urolift are not discharged with a catheter in situ.

In contrast, after the Rezum procedure, a urinary catheter is left in place for 5 to 7 days to allow the dead prostate tissue to drain away [NICE guidance MTG49]. The need for catheterisation, combined with the presence of necrotic tissue, are considered by the clinical experts to be predisposing factors for developing UTIs and, more rarely, urosepsis [NICE guidance MTG49]. This risk is higher for Rezum than UroLift, which usually does not need a post-operative urinary catheter [NICE guidance MTG49]. The clinical experts estimated that the risk of UTIs associated with a urinary catheter is around 5% to 7%, so a short course of prophylactic antibiotics may be prescribed after the procedure [NICE guidance MTG49]. Real-world outcomes for Rezum suggest an infection rate as high as 17% [Mollengarden 2018].

10. Economic modelling

A cost consequence decision tree model was commissioned from Heron in 2014 to support the submission for Medical Technologies Guidance by the manufacturer Neotract (now Teleflex). This model has now been updated by the manufacturer using the most recent clinical and cost assumptions and to enable modelling of the current pathway for Urolift. Following the decision by NICE to include Rezum as a comparator, further adaptations to the model have been made to accommodate this.

10.1 Model Structure

Model Overview

The cost consequence model examines two different scenarios for Urolift to reflect the established current day case pathway and the new emerging pathway where Urolift is being performed under a pure local anaesthetic, without an anaesthetist present and in an ambulatory setting:

Scenario 1: Day case surgery under local anaesthetic with or without light sedation

Scenario 2: Outpatient / ambulatory setting under pure local anaesthetic without anaesthetist

The cost consequence model assumes equal efficacy between all comparators. The aim of the model is to capture aspects of treatment which are likely to have resource use implications for the NHS.

Resource implications which the model considers include:

Procedure costs: differences in cost of equipment, duration of procedure, necessary staffing to perform the procedure, location in which the procedure is performed (theatre or outpatient / ambulatory procedure room) and length of stay in hospital.

Consumables costs: differences in the cost and number of consumables needed to perform a procedure

Complication costs: differences in the frequency and costs of common complications associated with the procedures

Follow up costs: Differences in the post procedure care pathways.

Resource implications which the model does not considers include:

Pre-procedure activity is assumed to be the same between Urolift and the comparators (as was the case in 2014) and have therefore been excluded.

However, in the Outpatient scenario, it could be reasonably assumed that a pre-op assessment would not be required and would therefore remove the need for a nurse-led outpatient appointment. This has not been modelled, but would further add to the efficiency and cost savings afforded by this scenario.

Structure

The model follows the same decision tree structure as the original model, with patients undergoing an initial treatment and a secondary procedure in the event of unsatisfactory symptom relief.

Comparators

The model has the same comparators as the original monopolar TURP, bipolar TURP and HoLEP. It also includes Rezum, which was added to the scope of the guidance update.

Perspective, time horizon

The model looks at direct medical costs to the NHS.

The time horizon has been changed from three years to five years to accommodate the latest clinical evidence from the LIFT trial which provided efficacy data for the 2015 model.

Model assumptions and inputs

Model assumptions are the same as in the original model, except that pre-procedure activity is now assumed to be the same (as was the case in 2014) and have therefore been excluded. Erectile and ejaculatory dysfunction have been excluded as the original model did not feature costs for them, only frequencies. Retreatment rates from the LIFT study at 5 years were 13.6% (19/140), with 31.5% (6/19) of those retreated being retreated with Urolift [Roehrborn 2017].

Since the initial guidance was published in 2015 recommending that Urolift be performed in a day-case setting, this pathway is now well established in NHS hospitals that offer Urolift. More recently, many hospitals are transitioning or looking to transition their service to offer Urolift in an ambulatory or outpatient setting under a local anaesthetic without sedation. To reflect new ways of working and the direction of travel in the way the Urolift pathway is evolving in the NHS towards an outpatient setting, the current model has included this optimal pathway as a separate scenario, making clear the significant resource reductions available.

Due to the quick recovery and lack of post-procedural complications, most NHS providers of Urolift have switched to telephone consultations post operation rather than face-to-face outpatient appointments. The model assumes this as the most efficient

follow-up schedule, also consistent with an expected desire to reduce physical hospital visits post COVID-19.

The 2014 modelling assumed that the average number of Urolift devices used per procedure would be 4. The latest real world data from on-going collection [redacted] carried out by NHS hospitals over the past three years, indicates that the mean number of implants used in NHS patients is 3.5 (SD ±1). Procedure times available from the same [redacted] indicate that the procedure is now being performed much faster than was conservatively estimated in 2014. Mean procedure time in NHS trusts over the past three years is 14 minutes (SD ±5 mins).

New data submitted for consideration in this guidance update shows that Urolift can be used to treat patients with an obstructive middle lobe. 5.3% of randomised patients in LIFT were rejected due to an obstructive median lobe, which was a contraindication at the time of that study [Rukstalis 2019]. There is not a strong source of epidemiological data in the literature to better predict the middle lobe prevalence so the assumption in this model has been taken from the LIFT study. The recent Medlift study using Urolift to treat middle lobes showed an increased use of 1.3 devices in treating middle lobe patients [Rukstalis 2019] and this has been assumed to be the case within this analysis. This estimate is also supported by surgeons in the UK who have performed Urolift on patients with obstructive middle lobes.

The model also now includes Rezum, using assumptions for Rezum that were used in the economic modelling for the recently published NICE guidance MTG49 [Rezum MTG49].

The price for Urolift used in the updated model is the list price of [redacted].

10.2 Model Variables

Name	Description	Value	Source
c_compRet	cost to treat acute urinary retention	£3,061.79	Rezum Medical Technology Guidance 2020 (MTG49) – Supporting Documentation
c_compStric	cost to treat stricture	£504.84	68% at £309; NHS Ref costs 2017-18; Day case HRG LB15E Minor bladder procedures, 19 years and over + 32% at £921 NHS Ref costs 2017-18; Elective inpatient HRG LB15E Minor bladder procedures, 19 years and over.
c_compTrans	cost to treat bleeding requiring transfusion	£348	Updated cost from MTG26
c_compTURS	cost to treat TUR syndrome	£2,102	2 days in high dependency ward (£693.00) and 2 days in normal ward £358.00 NHS reference costs 2017-18
c_compUTI	cost to treat UTI	£781	Updated from MTG26 NHS reference costs 2017/2018 LA04S
c_consumablesBTURP	cost of consumables used in Bipolar TURP procedure	£256.74	Source: NICE MTG 29 Greenlight Laser Bi-TURP includes: • 1 Bi-Loop per surgery, unit cost £189.34 plus 4 bags of glycine fluid, unit cost of £5.34, plus 0.5 roller ball pieces

			per surgery, unit cost £50 • 1 Ellik evacuator per patient, unit cost £21.04 • No capital or servicing costs
c_consumablesHoLEP	Cost of consumables used in HoLEP procedure	£448	Blended technology cost used in Rezum Medical Technology Guidance 2020 (MTG49) – Supporting Documentation
c_consumablesMTURP	Cost of consumables used in Monopolar TURP procedure	£88.44	From NICE MTG29 for Greenlight laser Mono-TURP includes: • 1 Mono-Loop per surgery, unit cost £52.60, plus 4 bags of glycine fluid, unit cost of £5.34, plus 0.5 roller ball pieces per surgery, unit cost £50 • 1 Ellik evacuator per patient, unit cost £21.04 • No capital or servicing costs
C_consumablesRezum	Cost of disposable, single use, Rezum treatment set	£1,348	Rezum Medical Technology Guidance 2020 (MTG49)
c_HCP_Anaesthtist	cost per minute of an anaesthetist	£1.82	PSSRU 2019. Table 14. Hospital-based doctors. Cost per hour = £109
c_HCP_band5Nurse	cost per minute of a band 5 nurse	£1.53	PSSRU 2019. Table 13. Hospital-based nurses. Band 5 nurse. Cost per hour patient contact = £92

c_HCP_healthcareAssist	cost per minute of a healthcare assistant	£0.36	Urolift update. EAC used £21.40 per hour (p7 of 15). Band 2 costs not available in PSSRU
c_HCP_Surgeon	cost per minute of the surgeon	£1.82	PSSRU 2019. Table 14. Hospital-based doctors. Cost per hour = £109
c_incont	cost per year to treat incontinence	£2,356.97	Inflated cost from MTG26; used in Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation
c_LOS_hospital	per day cost of inpatient hospital stay	£370.32	Accepted cost in Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation
c_medianLobe	Number of extra Urolift implants needed to treat obstructive median lobe	1.3	Number of extra implants used in Medlift study [Rukstalis 2019]
c_room_outpatient	cost per minute of an outpatient procedure room	£11	Estimated cost per minute based on the NHS Reference cost for an outpatient flexible cystoscopy: NHS Ref costs 2017-18; Urology HRG LB72A: £151. This provides an estimated cost per minute of around £11 per min for a 15 min procedure
c_room_theatre	cost per minute of an operating theatre	£14	PLICS 2016-17 https://analytics.improvement.nhs.uk/t/Public/views/PLICSPublicViewPrototype2016-

			17data/CostofNHSservices?iframeSizedToWindow=true&:embed=y&:showAppBanner=false&:display_count=no&:showVizHome=no
c_visit_OPconsultant	cost for outpatient consultation with a hospital consultant	£112	National Schedule of Reference Costs 2017/18; Urology O/P - consultant led
c_visit_OPnurse	cost for outpatient consultation with a hospital nurse	£94	Source: National Schedule of Reference Costs 2017/18; Urology O/P - non-consultant led
c_visit_telephoneconsult	cost for a nurse led telephone consultation	£15.7	Estimate based on 20 mins specialist nurse (Band 6). £47/hour. Source: Unit Costs of Health and Social Care. Personal Social Services Research Unit 2019
C_visit_TWOC	Cost for a trial without catheter outpatient visit	£144	Procedure code OPCS M47.3 Removal of urethral catheter from bladder. Maps to HRG LB15E. National Reference cost (2017/18) – Outpatient procedure (OPROC): £144
DevicesUsed	Number of Urolift devices used per procedure	3.5	Source: Data on file. [redacted] ***Appendix 2***. Also verified by local audits carried out by NHS users [NHS Fife 2020; [redacted]; Royal Devon & Exeter NHS Trust 2020; Norfolk & Norwich NHS Trust 2019]
c_deviceprice	Cost to purchase one Urolift device	[redacted]	Manufacturer provided

LOS_BTURP	post procedure length of hospital stay following bipolar TURP (days)	2.33	Source: Original NICE Guidance (EAC report p75). Same LOS was used in the more recent Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation
LOS_HoLEP	post procedure length of hospital stay following HoLEP (days)	1.98	Source: Original NICE Guidance (EAC report p75). Same LOS was used in the more recent Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation
LOS_MTURP	post procedure length of hospital stay following monopolarTURP (days)	3.03	Source: Original NICE Guidance (EAC report p75). Same LOS was used in the more recent Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation
LOS_PUL	post procedure length of stay following Urolift (days)	0.125	This LOS was agreed and used in the final base case for the Urolift NICE guidance (MTG26; pages 11 and 92 https://www.nice.org.uk/guidance/mtg26/documents/urolift-for-treating-lower-urinary-tract-symptoms-of-benign-prostatic-hyperplasia-assessment-report2). This length of stay (routinely 3 hours) has been confirmed in numerous reports from NHS hospitals. This LOS was also used by the EAC for the day case scenario in the recent Urolift guidance review (p11 of 15)
LOS _Rezum	post procedure length of stay following Urolift (days)	0.5	Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation

theatretime			
theatretime_BTURP	time in operating theatre for bipolar TURP (mins)	66	Source: Original NICE Guidance (EAC report p75). Same procedure time was used in the more recent Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation (p126-127)
theatretime_HOLEP	time in operating theatre for HoLEP (mins)	80.2	Source: Original NICE Guidance (EAC report p75). Same procedure time was used in the more recent Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation (p126-127)
theatretime_MTURP	time in operating theatre for monopolar TURP (mins)	66	Source: Original NICE Guidance (EAC report p75). Same procedure time was used in the more recent Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation (p126-127)
theatretime_PUL	time in theatre or procedure room for Urolift procedure (mins)	14	Source: Data on file. [redacted] collected from NHS trusts over past 3 years. Details supplied separately; ***Appendix 2***
theatretime_Rezum	time in theatre or procedure room	17.5	Rezum Medical Technology Guidance 2020 (MTG49), Supporting Documentation

	for Urolift procedure (mins)		

10.3 Efficacy Inputs

Beta distributions of probability for all variables derived from clinical data have been included in the model allowing PSA calculations to be performed

Name	Description	Value	Source
Prob_failPUL	probability of PUL failure at 5 years	13.6%	Roehrborn 2017
Prob_failBTURP	probability of bipolar TURP failure at 5 years	6%	Lourenco 2008*
Prob_failHOLEP	probability of HOLEP failure at 5 years	4.08%	Lourenco 2008*
Prob_failMTURP	Probability of failure for monopolar TURP at 5 years	6%	Lourenco 2008*
Prob_CompIncont_PUL	probability of incontinence after PUL	0	No reported instances of incontinence following Urolift procedure
Prob_CompRet_PUL	probability of acute retention after PUL	0.4%	Roehrborn 2017

Prob_CompUTI_PUL	probability of UTI after PUL	0.1%	Roehrborn 2017
Prob_CompIncont_TURP	probability of incontinence after TURP	3%	Lourenco 2008*
Prob_CompRet_TURP	probability of acute retention after TURP	5%	Lourenco 2008*
Prob_CompStric_TURP	probability of stricture after TURP	7%	Lourenco 2008*
Prob_CompTURS_TURP	probability of TUR syndrome after TURP	3%	Lourenco 2008*
Prob_CompUTI_TURP	probability of UTI after TURP	6%	Lourenco 2008*
Prob_CompTrans_TURP	probability of blood transfusion after TURP	8%	Lourenco 2008*
Prob_CompIncont_HOLEP	probability of incontinence after HOLEP	2.91%	Lourenco 2008*
Prob_CompRet_HOLEP	probability of acute retention after HOLEP	3.55%	Lourenco 2008*
Prob_CompStric_HOLEP	probability of stricture after HOLEP	5.88%	Lourenco 2008*
Prob_CompTURS_HOLEP	probability of TUR syndrome after HOLEP	0.93%	Lourenco 2008*
Prob_CompTrans_HOLEP	probability of blood transfusion after HOLEP	2.16%	Lourenco 2008*
Prob_CompUTI_HOLEP	probability of UTI after HOLEP	5.88%	Lourenco 2008*
P_medianLobe	Probability that patient will have an obstructive median lobe that requires treatment	5.3%	Rukstalis 2019
Prob_failRezum	Probability of Rezum failure at 5 years	4.4%	McVary 2020

Prob_CompRet_Rezum	Probability of acute retention after Rezum	0.5%	McVary 2016
Prob_CompStric_Rezum	Probability of Stricture after Rezum	1.1%	McVary 2016
Prob_CompUTI_Rezum	Probability of UTI after Rezum	2.1%	McVary 2016
P_TWOC_Rezum	Probability patient has to return for a catheter removal post procedure	100%	Rezum Medical Technology Guidance 2020 (MTG49)

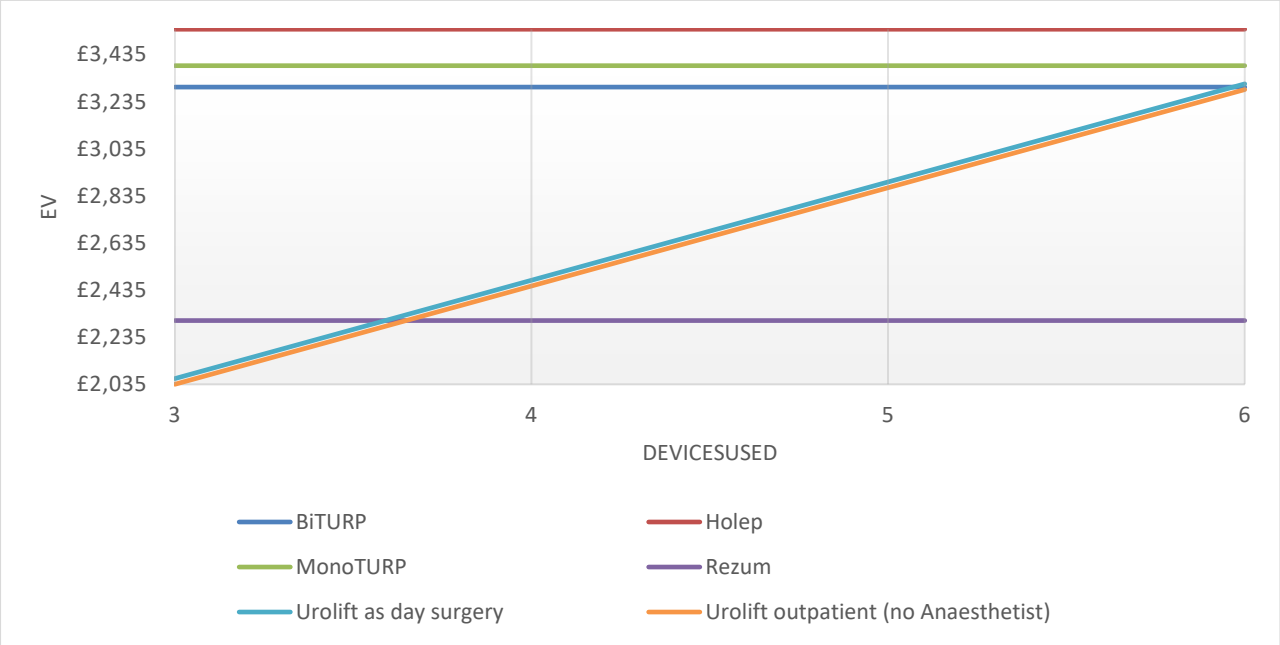
*Probability values were used in the original economic model for the Urolift NICE guidance MTG26 and accepted by the EAC at the time)

10.4 Results

Scenario	Per patient cost	Incremental cost vs. Urolift
Urolift – Outpatient setting (no Anaesthetist)	£2,240	£ -
Urolift – day case surgery	£2,265	£24
Rezum	£2,306	£66
BiTURP	£3,297	£1,057
MonoTURP	£3,388	£1,148
HoLEP	£3,543	£1,303

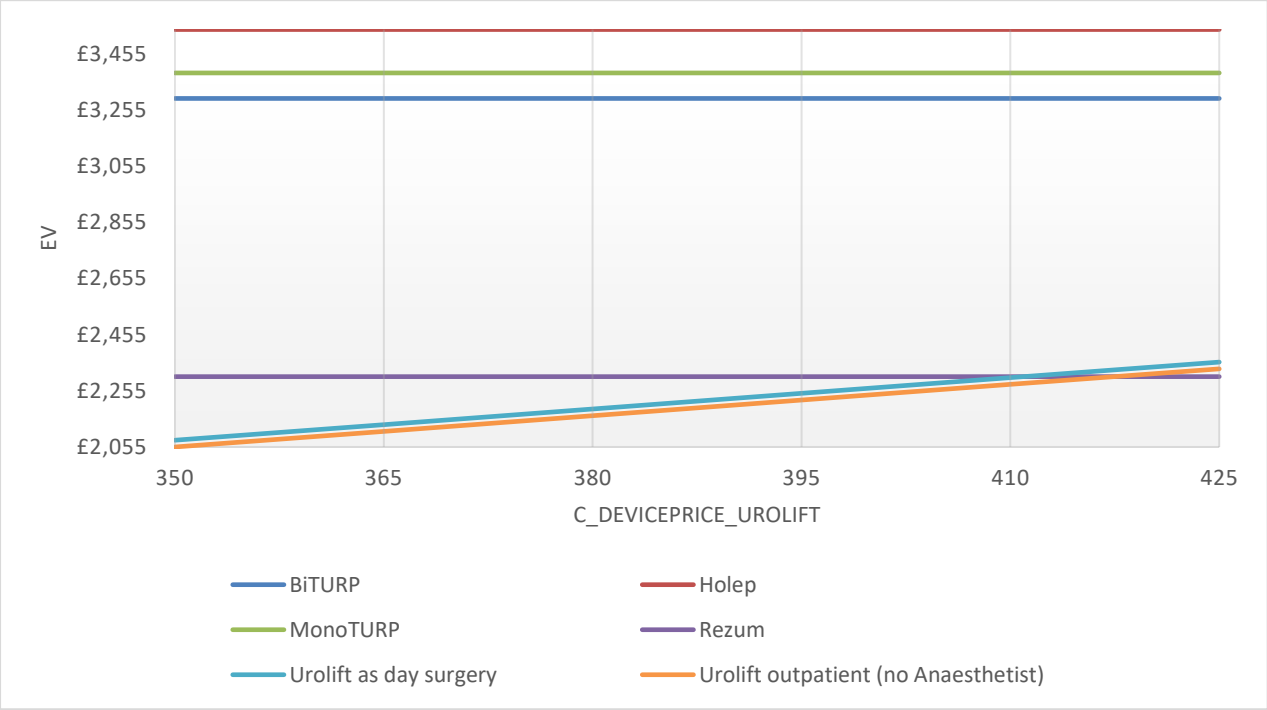
10.5 Sensitivity Analysis

One Way Sensitivity Analysis: Number of Urolift Devices Used



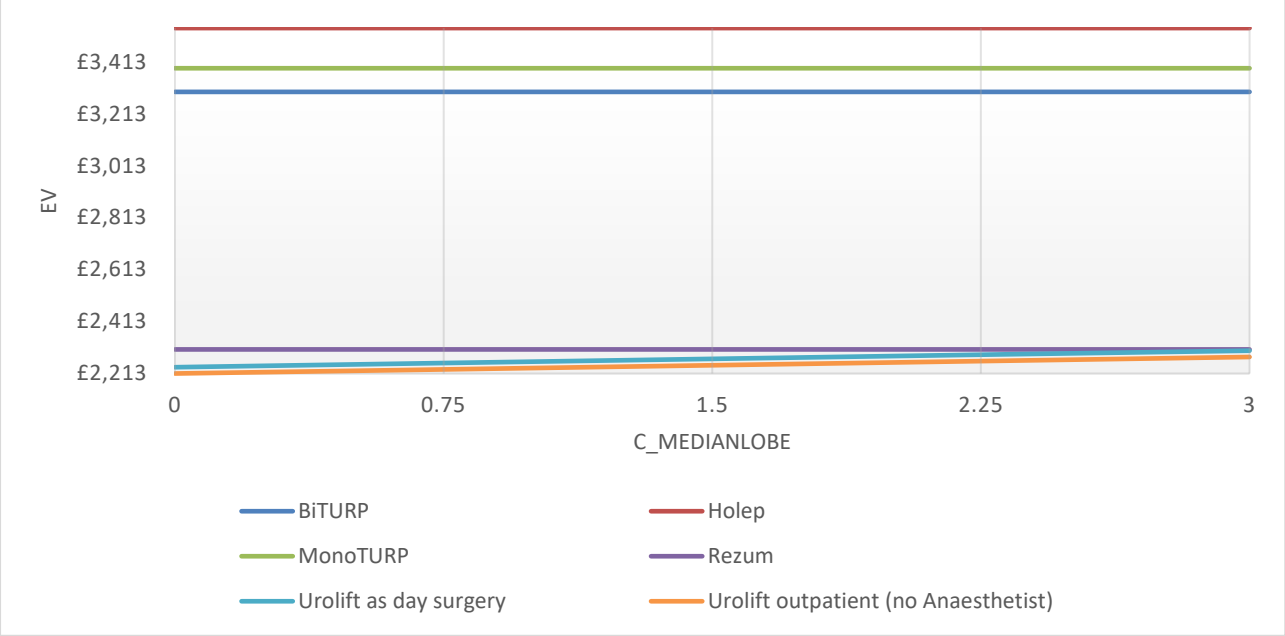
Rezum becomes a cheaper option once the average number of Urolift devices used exceeds 3.65. Urolift remains cheaper than other treatment options in the simulated range.

One way Sensitivity analysis: Price of Urolift Devices



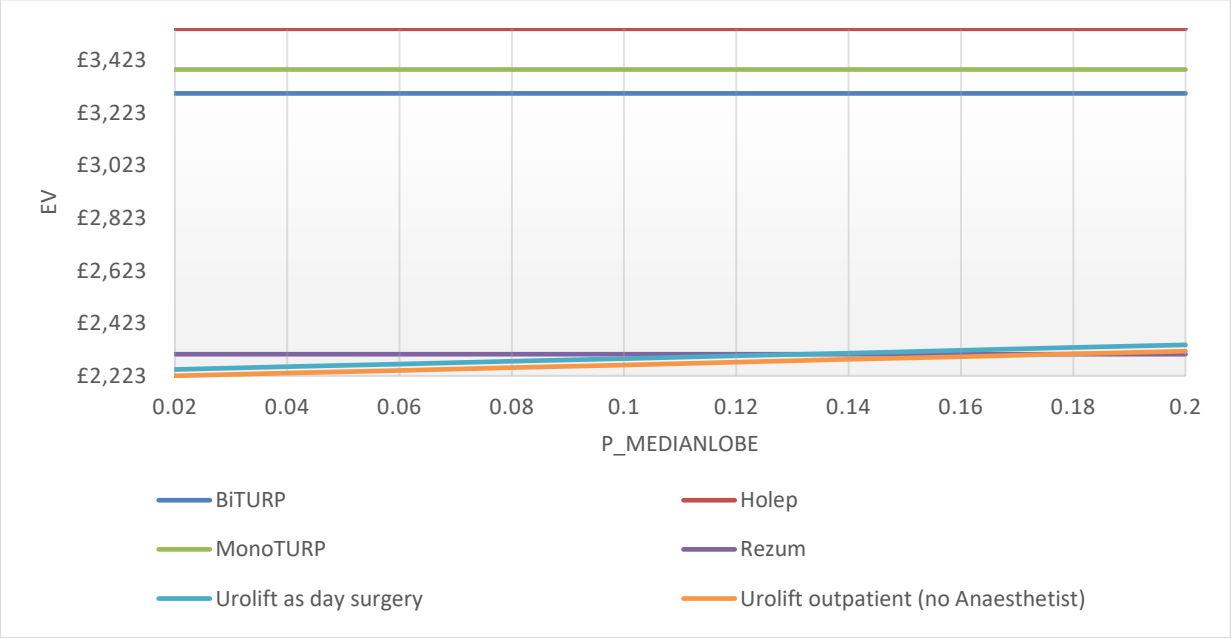
Rezum becomes the cheaper option when average price of Urolift devices exceeds £417.55. Urolift remains cheaper than other treatment options across the simulated range

One way Sensitivity analysis: Number of extra devices needed to treat patients with a median lobe



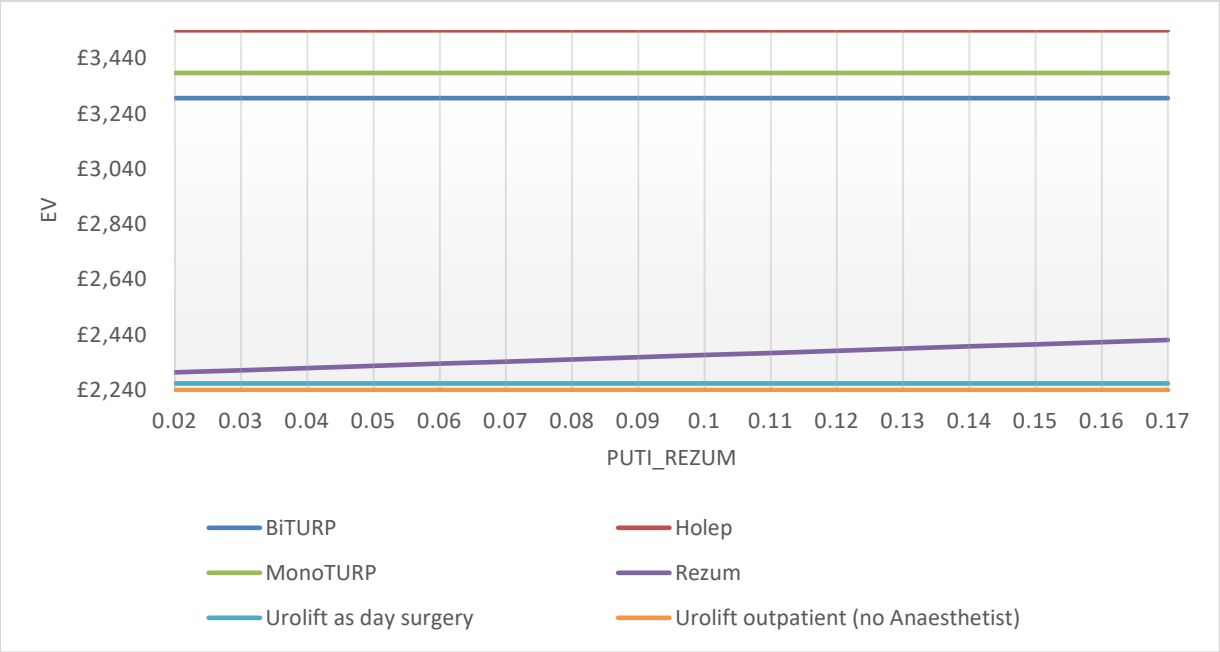
Urolift remains cheaper than all treatment options across the simulated range.

One way Sensitivity analysis: Probability of patients having a median lobe



Rezum becomes a cheaper option if the incidence of patients presenting for treatment with a median lobe is above 17.8%

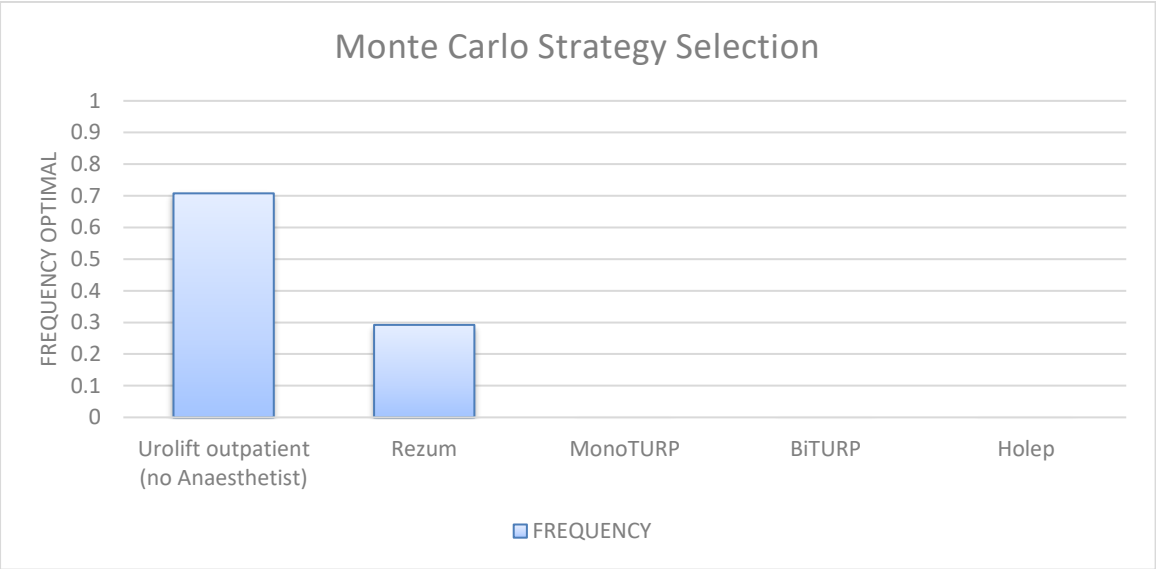
One way Sensitivity Analysis: Probability of UTI following Rezum



At the upper range of reported incidence of UTI with Rezum (17%; Mollengarden 2018) the cost increases to £2,421 per patient.

Probabilistic Sensitivity Analysis

PSA results indicate that Urolift will be cheaper than the next cheapest comparator in 59.4% of 10,000 model iterations.



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12. Patient testimonials

Teleflex has provided testimonials from 13 patients who have been treated with Urolift. These are provided in **Appendix 5.**

Teleflex has also provided **(Appendix 6)** a list of 13 patients who have treated with Urolift and who have given their express permission for the company to share their contact details with NICE and to be contacted by NICE about their experience.

13. Declaration:

Company representative: Matt Wiggins

Position: General Manager EMEA

date: 17 July 2020

14. Appendices

Appendix 1. Procedure Numbers by NHS Trust

Appendix 2. Urolift patient tracker data

Appendix 3. NHS hospitals/users

Appendix 4. Economic model

Appendix 5. Urolift patient testimonials

Appendix 6. List of Urolift patients and contact details

NICE National Institute for Health and Care Excellence

Medical technologies guidance

Collated expert questionnaires

Technology name & indication: **MT241 UROLIFT SYSTEM for treating lower urinary tract symptoms of benign prostatic hyperplasia**

Experts & declarations of interest (DOI)

Expert #1	Ian Pearce, Consultant Urological Surgeon, Manchester University NHS Foundation Trust, British Association of Urological Surgeons
	DOI: None
Expert #2	Tamer El-Husseiny, Consultant Urological Surgeon, Imperial College Healthcare NHS Trust, GMC, BMA, European Association of Urology, Endourological Society
	DOI: None
Expert #3	Maya Harris, Consultant Urologist, South Warwickshire NHS Foundation Trust, BAUS, AUA, EAU, Royal College of Surgeons of England
	DOI: None

How NICE uses this information: the advice and views given in these questionnaires are used by the NICE medical technologies advisory committee (MTAC) to assist them in making their draft guidance recommendations on a technology. It may be passed to third parties associated with NICE work in accordance with the Data Protection Act 2018 and data sharing guidance issued by the Information Commissioner's Office. Expert advice and views represent an individual's opinion and not that of their employer, professional society or a consensus view (unless indicated). Consent has been sought from each expert to publish their views on the NICE website.

For more information about how NICE processes data please see our privacy notice.

1. **Please describe your level of experience with the technology, for example: Are you familiar with the technology? Have you used it? Are you currently using it? Have you been involved in any research or development on this technology? Do you know how widely used this technology is in the NHS?**

Expert #1	I am very familiar with the technology and have been using it in my clinical practice for over 2 years. I have been trained both here in the UK and in Madrid and continue to offer this to my patients I have not been involved in any research relating to Urolift, but am in the process of developing an out patient local anaesthetic service. I understand that Urolift is now offered in over 95% of UK NHS hospital Trusts
Expert #2	I have been regularly performing Urolift insertions for almost 4 years now and I am still performing it. I was one of the early adopters of this technology in the UK. It is currently widely used across different units on the NHS. I am currently working on a systematic review for recent BPH treatment modalities.
Expert #3	I am very familiar with the technology and started performing the procedure one of the first in the region (West Midlands). I continue offering Urolift procedure to the patients. I have not been involved in the research and development of the procedure. I am aware of a few NHS centres which are offering Urolift procedure.

2. **Has the technology been superseded or replaced?**

Expert #1	No
Expert #2	Other treatment modalities have been introduced such as the Rezum water vapour therapy & the Aquablation – but have not replaced or superseded the Urolift.

Expert #3	There are some procedures which could be considered for the same population of the patients looking for a minimally invasive surgery for lower urinary tract symptoms (e.g. Rezum).

Current management

3. How innovative is this technology, compared to the current standard of care? Is it a minor variation or a novel concept/design?

Expert #1	This is a novel concept designed to achieve what would previously require a much more invasive operation with a much greater side effect profile
Expert #2	It is an innovative and novel technology
Expert #3	Urolift is one of the most innovative procedures in urology, as it has changed the concept of prostatic surgery.

4. Are you aware of any other competing or alternative technologies available to the NHS which have a similar function/mode of action to the notified technology? If so, how do these products differ from the technology described in the briefing?

Expert #1	Whilst not the same technology, Rezum is a newly introduced method of achieving the same end outcome of relieving prostatic mediated bladder outflow obstruction. This technology involves utilising steam which is injected directly into the prostate to cause thermo-destruction and hence a reduction in prostatic tissue thus relieving obstruction
Expert #2	None
Expert #3	I am not aware of similar technologies.

Potential patient benefits

5. What do you consider to be the potential benefits to patients from using this technology?

Expert #1	Minimally invasive Shorter hospital stay Fewer complications Instantly effective No requirement for post operative catheter
Expert #2	- Performed under local anaesthesia + sedation - Day case - No sexual side effects - Early improvement of symptoms - No postoperative urinary catheter
Expert #3	The potential benefits are minimally invasive Day Case procedure, minimal risk of incontinence and strictures, and preservation of sexual function.

6. Are there any groups of people who would particularly benefit from this technology?

Expert #1	Patients at high anaesthetic risk and those who have yet to complete their family
Expert #2	Suitable for both: - Younger patients – to preserve sexual function - Older patient who are unfit for undergoing other BPH interventions under general anaesthesia.
Expert #3	Patients who are young (as sexual function preservation is important) and older patients who would like to avoid hospital admission and risk of blood transfusion, incontinence and stricture

7. Does this technology have the potential to change the current pathway or clinical outcomes? Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?

Expert #1	Yes Less invasive therapy Potential for out patient delivery of care

Expert #2	Yes it could improve the current pathway - Minimally invasive surgery - Day case procedure under local + sedation - Minimal side effects - Improved outcomes.
Expert #3	It has certainly changed the pathway with less hospital admissions and less invasive treatment.

Potential system impact

8. What do you consider to be the potential benefits to the health or care system from using this technology?

Expert #1	Shorter hospital stay Lower financial burden secondary to complications Less theatre time
Expert #2	- Day case procedure - Short procedure (approximately 15 minutes) - Improve theatre utilisation - Save on LOS and hospital beds - Less catheter related problems in the community - Minimal side effects. - Less readmission rates.
Expert #3	Reduced cost (as the theatre time and admission is shorter), reduced readmissions with complications.

9. Considering the care pathway as a whole, including initial capital and possible future costs avoided, is the technology likely to cost more or less than current standard care, or about the same?

Expert #1	Financial models show this to be cost effective, largely on the basis of reduced in patient stay

Expert #2	Likely to be cost saving.
Expert #3	I think the overall costs would be the same.

10. What do you consider to be the resource impact from adopting this technology? Could it, for example, change the number or type of staff needed, the need for other equipment, or effect a shift in the care setting such as from inpatient to outpatient, or secondary to primary care?

Expert #1	A realistic option is to see a shift in the care delivery setting from in patient to out patient
Expert #2	Only the kit – endoscope & the Urolift implants are required. Otherwise, no additional resources are needed. Will free up inpatient beds as it is carried out as a day case procedure.
Expert #3	It does require specialised equipment (cystoscopes) and consumables. Minimal additional staff training is required if the surgeon is trained in the procedure.

11. Are any changes to facilities or infrastructure, or any specific training needed in order to use the technology?

Expert #1	No changes to infrastructure Training for the clinician and theatre staff required
Expert #2	No change from the existing setup.
Expert #3	Mostly surgeon's training and specialised cystoscopes (however those were provided by the company for all cases which I have performed)

12. Are you aware of any safety concerns or regulatory issues surrounding this technology?

Expert #1	No
Expert #2	None

Expert #3	I am not aware of any safety concerns

General advice

13. Please add any further comments on your particular experiences or knowledge of the technology, or experiences within your organisation.

Expert #1	Easy to master the technique Widely accepted by patients
Expert #2	- Very good technology. Effective. Minimal side effects. - Special caution should be taken when used in patients with high risk for prostate cancer who might need future MRI scans of the prostate given the artefact appearance produced by the implants on the MRI images. - Not suitable for patients with obstructing middle lobe of the prostate. - Not suitable for patients with chronic urinary retention.
Expert #3	One of the challenges of this technology is the patient selection, as it is not suitable for patients in chronic retention and prostates of a certain shape (presence of middle lobe). It is also not suitable if the patient had radiotherapy for prostate cancer.

Other considerations

14. Approximately how many people each year would be eligible for intervention with this technology, either as an estimated number, or a proportion of the target population?

Expert #1	15,000 in the UK approx
Expert #2	I expect 20-30% of bladder outflow surgeries could be offered a Urolift.
Expert #3	I estimate about 10-15% of patients presenting with prostate problems (if urinary retention patients are included). In a younger population presenting with symptoms only, up to 40-50% could be suitable.

15. Would this technology replace or be an addition to the current standard of care?

Expert #1	Largely replace TURP but likely to be offered in addition to
Expert #2	In addition to other treatment options such as the Rezum and the HoLEP, not instead
Expert #3	I think it is a valuable option in the portfolio of treatments offered (conservative management, Rezum, TURP, laser prostatectomy)

16. Are there any issues with the usability or practical aspects of the technology?

Expert #1	No
Expert #2	- Training of staff - Preoperative flexible cystoscopy to rule out an obstructing middle lobe.
Expert #3	Patient selection is important

17. Are you aware of any issues which would prevent (or have prevented) this technology being adopted in your organisation or across the wider NHS?

Expert #1	No
Expert #2	None
Expert #3	Managerial reluctance, as the Urolift implants are costly.

18. Are you aware of any further evidence for the technology that is not included in this briefing?

Expert #1	No
Expert #2	None
Expert #3	No

19. Are you aware of any further ongoing research or locally collected data (e.g. audit) on this technology? Please indicate if you would be able/willing to share this data with NICE. Any information you provide will be considered in confidence within the NICE process and will not be shared or published.

Expert #1	No
Expert #2	The PULSAR study data looking in to outcomes of Urolift in patients with acute retention.
Expert #3	I have recently submitted departmental data to British Association of Urological Surgeons BOO audit, which is yet to report. The audit included a snapshot of all procedures performed for benign prostatic hyperplasia in November 2019, including Urolift.

20. Is there any research that you feel would be needed to address uncertainties in the evidence base?

Expert #1	The impact of the implants on the MRI finings in men presenting after the operation with raised PSA
Expert #2	Prospective RCT's comparing the newer treatments head to head such as the Rezum Vs Urolift & Aquablation etc.
Expert #3	Independent research to improve patient selection for the procedure

Declaration of interests

Description of Interest	Date Interest arose	Date Interest ceased
Ian Pearce: *Non-financial professional NICE advisor on Rezum 2019*		

Please see over the page information on how to complete the above boxes

The information you provide on this form will be used to assess if you have any potential conflicts of interest, we ask for this information to comply with our organisational policies.

Information may be disclosed to third parties in accordance with the Freedom of Information Act 2000 and will be published in registers that NICE holds.

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I confirm that the information provided above is complete and correct. I acknowledge that any changes in these declarations during the course of my work with NICE, must be notified to NICE as soon as is practicable and no later than 28 days after the interest arises. I am aware that if I do not make full, accurate and timely declarations this may result in potential disciplinary action if there has been a deliberate breach of the policy.

I do / do not [delete as applicable] give my consent for this information to be published on the registers that NICE holds. If consent is NOT given, please give reasons below: (please note this will be agreed in exceptional cases only).

Reason for non-disclosure: Enter text here.

Signed (employee): Enter text here. **Date:** Enter text here.

HOW TO COMPLETE THE DECLARATION OF INTEREST FORM

Name & role: Insert your name, your role and employer within the NHS.

Description of Interest: Provide a description of the interest that is being declared. This should contain enough information to be meaningful to enable a reasonable person with no prior knowledge to be able to read this and understand the nature of the interest.

Types of interest:

Financial interests - where a person gets direct financial benefit.

Non-financial professional and personal interests - Where a person has role relevant to NICE's work from which they do not receive a financial benefit. This includes:

- holding office or a position of authority in a professional organisation such as a Royal College, a university, charity, advocacy group or any other organisation in the health, public health or care sector

- holding a position of authority in an organisation contracting for services with NICE.

Indirect interests - where there is, or could be perceived to be, an opportunity for a third party closely associated with the board member or employee to benefit.

A benefit may arise from both a gain or avoidance of a loss.

Relevant Dates: Detail here when the interest arose and, if relevant, when it ceased.

NICE National Institute for Health and Care Excellence

National Institute for Health and Care Excellence
Centre for Health Technology Evaluation

Pro-forma Response

External Assessment Centre Report factual check

Urolift guidance update MT241

Please find enclosed the assessment report prepared for this assessment by the External Assessment Centre (EAC).

You are asked to check the assessment report from [insert EAC] to ensure there are no factual inaccuracies contained within it. If you do identify any factual inaccuracies you must inform NICE by 12pm, **18th September 2020** using the below proforma comments table. All your comments on factual inaccuracies will receive a response from the EAC and when appropriate, will be amended in the EAC report. This table, including EAC responses will be presented to the Medical Technologies Advisory Committee and will subsequently be published on the NICE website with the Assessment report.

15th September 2020

NICE National Institute for Health and Care Excellence

Issue 1

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
The report does not currently include consideration of the evidence presented for use of Urolift in men with obstructing middle lobe (Rukstalis 2018). This evidence was considered in the Review Proposal Paper and Review Decision in November 2019.	Include consideration of the evidence for including men with obstructing middle lobes for treatment with Urolift Rukstalis D *et al.* Prostatic Urethral Lift (PUL) for obstructive median lobes: 12 month results of the MedLift Study. *Prostate Cancer Prostatic Dis* **22,** 411–419 (2019). https://doi.org/10.1038/s41391-018-0118-x	In the original guidance recommendations (MTG26 section 1.2), it states 'The UroLift system should be considered as an alternative to current surgical procedures …. in men … *without an obstructing middle lobe.* In the request for information by NICE, the company was asked if the technology has added new indications or is now used in new applications not covered by the original guidance. In its submission in July 2019, The company responded with '*UroLift can now be performed in men with an obstructing middle lobe. Clinical evidence for this is supported by Rukstalis et al 2018. Patients with obstructing middle lobes are now being routinely offered Urolift in NHS hospitals'* The Review Decision (Nov 2019) was to Update the guidance to allow the MTAC committee to consider changes in the estimated costs and clinical considerations for using UroLift in day case procedures and *in people with obstructing middle lobes*.	Paper added

		The Review Proposal paper (Nov 2019) states: *Evidence from a prospective, non-randomised US study evaluating the safety and effectiveness of the prostatic urethral lift (PUL) in 45 men with middle and median lobe characteristics (Rustalis et al. 2018), suggested that men with BPH including those with middle lobe obstruction, can be treated with the PUL procedure safely and effectively.*	

Issue 2

Description of factual inaccuracy	**Description of proposed amendment**	**Justification for amendment**	**EAC response**
Consideration and modelling of a scenario where the length of stay for Urolift and Rezum are similar is not supported by the evidence	Remove consideration of scenarios where Urolift and Rezum have the same length of stay	Despite the assumptions in MTG49 that Urolift and Rezum have a comparable Length of Stay (LOS), the company would like to present evidence in the form of Hospital Episode Statistics (2018-20; presented as Appendix 1 to these comments), which provides Length of Stay (LOS) for procedures identified through OPCS coding as exclusively Urolift or Rezum. The data shows a clear difference in the LOS between Urolift and Rezum, suggesting that the LOS of Rezum is as much as 3 times that of Urolift. In the base case for the Urolift guidance (MTG26; pages 11 and 92 https://www.nice.org.uk/guidance/mtg26/documents/urolift-for-treating-lower-urinary-tract-symptoms-of-benign-prostatic-hyperplasia-assessment-report2) a LOS for Urolift of 0.125 days is used and this was pointed out in the comments submitted by Teleflex in the consultation for	MTG49 stated that there was no published data for the length of stay. There was wide agreement that Rezum could normally be carried out as a daycase. The accepted MTG26 model included 0.5 days and also daycase surgery which had a length of stay of 0.125 days The EAC are unable to exactly replicate the HES data for combined codes, however note that correspondence for Rezum identified poor reliability of HES

		MTG49. It has never been part of the assumptions or part of the expert feedback for Rezum (during the development of MTG49) that LOS of Rezum could be as low as 0.125 days. As Rezum is performed in the NHS under general anaesthesia or local anaesthesia with sedation, it would be unrealistic to expect patients to be discharged within 2-3 hours (as is the case with Urolift). This is supported by the HES data presented.	due to the issues of coding for the procedure. The scenario has been left in place, however text has been changed to highlight that this is an exploration of assumptions, and that there is no evidence to suggest that Rezum length of stay is as short as 0.125 days. Additional change to: p.9: Urolift only remains cost saving compared to Rezum, where the key company assumptions are accepted, including a shorter length of stay. p. 75 The first scenario included is for a reduced LOS for Rezum (0.125 days, or 3 hours) based on an assumption from MTG49, however there is no evidence for this reduced length of stay, the scenario is intended to explore the direction of uncertainty. HES data

			submitted by the company during fact check indicates a length of stay of 0.87 days, however there absence of a specific code for use of Rezum reduces confidence in this figure. No data for length of stay was identified for Rezum during MTG49.

Issue 3

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
The company would like to submit for inclusion, a recently accepted abstract from NHS Fife on the use of Urolift under local anaesthetic without the presence of an anaesthetist. Please refer to Appendix 2		This abstract was not available for submission in July when the submission pack was provided to NICE	Results are largely included in existing table for NICE shared learning case studies. Abstract referenced as footnote.

Issue 4

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 10 of 95. Typically about 4 implants are used.	Typically, a range of 2-5 implants are used; average 3.5.	The company submitted [redacted]	Changes made

NICE National Institute for Health and Care Excellence

Issue 5

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 11 of 95: Misrepresentation of the clinical guidelines for LUTS in this context (page 11 of 95).*The clinical guideline also recommends offering adjustable prostatic implants (such as the UroLift system) for the treatment of storage symptoms only as part of a randomised controlled trial*	Remove reference to adjustable prostatic implants or Urolift for the treatment of storage symptoms Remove reference to the treatment of storage symptoms	1. Consideration of treatments for storage symptoms is out of scope for this guidance which considers only treatments for <u>voiding</u> symptoms of BPH. 2. NICE Clinical Guideline CG97 (para 1.6.7) states '*consider offering intramural injectables, implanted adjustable compression devices and male slings to manage stress urinary incontinence only as part of a randomised controlled trial. [2010]'.* It should be noted that the clinical guideline is not describing adjustable prostatic implants in this instance. Adjustable compression devices described in this guideline are not related in any way to the Urolift technology, which is a prostatic implant. To our knowledge, the use of prostatic implants (eg Urolift) for the treatment of <u>storage</u> symptoms has not been considered in any NICE guidance or clinical guidelines	This information was included in the NICE scope document for this guidance update. I believe it is for wider reference and so no changes have been made.

Issue 6

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 65 of 95: Additional scenario considered: BiTURP has day surgery, using LOS =0.5 days	Remove this scenario	This scenario is not supported by the evidence. HES data recorded 18,149 TURP procedures in 2019/20. Although it is not possible through the coding to differentiate between biTURP and monoTURP, only 996 (5.5%) of the overall TURP procedures were recorded as day case (0 LOS)	Additional explanation added p75: The third scenario sets biTURP length of stay at 0.5 days (or 12 hours) to explore the impact of biTURP being carried out as a daycase procedure. Included data and NHS patient information (NHS website) point to around 2 days being a typical length of stay currently, however there is evidence that it can be carried out as a daycase for some patients within the NHS (Lavan 2018). This scenario explores the potential impact if this were to become more widespread.

Issue 7

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response

Page 67 of 95: The key changes in the current submitted model for Urolift, compared to MTG49	Add to the list of key changes: the addition of a TWOC appointment to the pathway	A TWOC appointment was not included in the modelling for MTG49	The following statement has been added: • Additional trial without catheter (TWOC) appointment for Rezum (was included in some EAC scenarios for MTG49)

Issue 8

Description of factual inaccuracy	**Description of proposed amendment**	**Justification for amendment**	**EAC response**
Page 67 of 95: Reduced change in theatre time for Urolift from 30 to 14 minutes (included studies are between 8min and 1 hour, 4 are closer to an hour	It should be noted that the 4 studies where theatre time was closer to an hour were US studies and not reflective of current NHS practice	US clinical practice is not comparable to NHS practice, where efficiency is not incentivised or even encouraged in the same way as it is in the NHS	The studies reporting over 50 minutes were based in: USA, Canada, Australia, Denmark, UK, Germany, Italy The studies with the shortest times were based in: UK, Spain and Turkey The definition of the period timed is not given in the studies and there may be some differences between anaesthetic, procedure and operative or theatre time. The EAC have included a short table summarising the length of stay and procedure time for the different studies, and also added information

			from NICE Shared Learning Case studies. This is a summary of evidence presented in the clinical section.. Included at end of table.

Issue 9

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 67 of 95: Scenario included where all follow-ups by telephone consultation, for all comparators	Suggest remove this scenario	For treatments where patients are discharged with a catheter in situ (eg Rezum), patients will need to attend an in-clinic appointment for a TWOC	Text has been changed to clarify that although the follow-up appointment was changed to a telephone consultation for all comparators, the additional TWOC appointment remains in place for Rezum. No change in modelling was required. 'All follow-ups by telephone consultation, for all comparators. An additional TWOC appointment remains in place for Rezum.'

Issue 10

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 59 of 95. EAC update to the price of Urolift: [redacted]	Leave as *'No change'* from £[redacted]	In the completed 'Information Request from the Sponsor submitted by the company in July 2020 (page 4 of 47: provided here again as an appendix), the company stated: *The*	Text changed to "No change" and comment removed.

		current price of the Urolift implants is £[redacted] (ex VAT) per implant. This information updates and supersedes all information supplied in 2019	The cost used in the EAC base case was £[redacted], therefore no change in modelling required.

Issue 11

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 68 of 95. *Note* [redacted]	Remove this statement	In the completed 'Information Request from the Sponsor submitted by the company in July 2020 (page 4 of 47: provided here again as an appendix), the company stated: *The current price of the Urolift implants is [redacted] (ex VAT) per implant.* This information updates and supersedes all information supplied in 2019	This was in the context of sensitivity analysis exploring plausible ranges of cost. The statement has been clarified to: [redacted] has previously been quoted as the cost of individual device purchases in the 2019 cost update, but the current list price is £[redacted] per device.'

Issue 12

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 10 of 95. Section 3.	The current guidance (MTG26; section 2.2) states *Urolift can be done under local or general*	In its information submission to NICE in July 2020, the company stated that "*more and more trusts have either transitioned or are*	Changes made

The company states that UroLift can be performed under local anaesthetic, without an anaesthetist present, with light sedation if needed.	*anaesthetic.* The company states that UroLift is increasingly performed, in NHS hospitals, under local anaesthetic without sedation and therefore without the requirement for an anaesthetist to be present.	*looking to transition to a local anaesthetic only protocol, removing the need for an anaesthetist and paving the way to transition to an outpatient/ambulatory setting*' The company also included in this information submission (included as an appendix to this comments; page 9 of 47) a local anaesthetic protocol, which has been verified by 2 NHS users of Urolift.	

Issue 13

Description of factual inaccuracy	**Description of proposed amendment**	**Justification for amendment**	**EAC response**
Page 7 of 96: However, UroLift appears to be superior compared to Rezum for symptom severity and erectile dysfunction measures	However, UroLift appears to be superior compared to Rezum for symptom severity and erectile and ejaculatory dysfunction measures	Tutrone R.F. and Schiff W. Early patient experience following treatment with the UroLift prostatic urethral lift and Rezum steam injection. *CJU* **27** (3), 10213-10219 (2020) demonstrated that UroLift System patients reported better sexual function scores compared to Rezum patients. At least 30% better MSHQ-EjD score for ejaculatory function and up to 60% better SHIM scores for erectile function were recorded.	Changes made

Issue 14

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 10 of 96: intended for use … in men 45 years of age or older.	Change to 50 years of age or older	45 years is the US indication. It conflicts with the OUS indication listed on the next page of 50 years, which is relevant to UK and is consistent with the recommendations in the guidance MTG26	Changes made

Issue 15

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 15 of 95: Roehrborm et al (2015). EAC comments: Study was powered for the primary endpoint assuming a t-test comparison of mean values with 0.5 two-sided type 1 error and 80% statistical power	Should read: …. 0.05 two-sided type 1 error ….	Corrected according to the published paper	Changes made

Issue 16

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 15 of 95: Roehrborm et al (2015). Design and interventions: Prostate length measurement of ≥ 30mm and ≤ mm	Should read: Prostate length measurement of ≥ 30mm and < 80mm	Corrected according to the published paper	Changes made

Issue 17

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 17 of 95: Sonksen (2015). The BPH6 study. Participants and setting: n = 45 (46 randomised, 1 declined treatment),	Should read: n=44 (46 randomised, 1 declined treatment, 1 protocol deviation)	Corrected according to the published paper	Changes made

Issue 18

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 17 of 95: Sonksen (2015). The BPH6 study. Design and interventions: Qmax ≥15 ml/s for 125-ml voided volume Post-void residual volume ≤350 ml	Should read: Qmax ≤15 ml/s for 125-ml voided volume Post-void residual volume <350 ml	Corrected according to the published paper	Changes made

Issue 19

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response

Page 23 of 96: Bardoli et al (2017). Participants and setting: 11 patients from 53 identified who were eligible for TURP …	Should read: 11 patients from 52 identified who were eligible for TURP …	Corrected according to the published paper	Changes made

Issue 20

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 24 of 96: Roehrborn et al (2017). Participants and setting: 87/140 patients were available from the PUL group at 5 years	104/140 patients were available from the PUL group at 5 years	140 total patients were randomized to the PUL group and at 5-year follow up, 36 patients were not available due to lost to follow up, unrelated death, cancer treatment and willing exit following TURP. This left **104** patients available for follow up. Of the 104 available subjects, 17 were censored for TURP/Laser/UroLift retreatment or protocol deviations, leaving **87** to be included in the per protocol analysis. Authors performed both Intent to Treat (ITT) and Per Protocol (PP) analyses and showed no difference in efficacy outcomes.	Have not changed the figures as feel it is misleading to include the 104 figure as this is not what was used for analysis. Have added '87 were available for analysis'.

Issue 21

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response

Page 24 of 96: Roehrborn et al (2017). Outcomes: MSHQ-EjD	Should read: IIEF-5 instead of MSHQ-EjD	Corrected according to the published paper	It is the IIEF-5 as well as the MSHQ-EjD so have added it to the outcomes list.

Issue 22

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 27 of 96. Tutrone and Schiff (2020): Questionnaires completed an average of 30 days post procedure	Also included questions around urinary catheter experience, recovery, interference with daily activities, BPH medication use and treatment satisfaction.	Corrected according to the published paper	As the scope does not specify patient experience and satisfaction with the treatment, these outcomes are outside of scope and no changes have been made.

Issue 23

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 29 of 96. Section 5.2 Some concerns were identified in the non-comparative studies …. or no inclusion/exclusion criteria (Eure et al; 2019 and Sievert et al; 2019),	Remove reference to Eure et al and Sievert et al in this context	Both Eure et al and Sievert et al are real world retrospective registry studies, with enrolment in line with that is real-world clinical practice. These studies support safety and efficacy in broad patient populations.	The issues identified are not incorrect so no changes have been made.

Issue 24

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 30 of 96. Table 4 Direction of improvement in scores for QoL: Increase	Add: If QoL is IPSS Q8 then a *decrease* signifies improvement	Clarity for the reader	Table already says decrease for QoL so no changes have been made.

Issue 25

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response

Page 31 of 96. Roehrborn et al (2015). Erectile and sexual dysfunction (MSHQ, MSHQ-EjD, IIEF and SHIM) column: *Not reported*	Details should read: No significant differences in change in SHIM score from baseline UroLift and TURP at any of the follow-up time points. Significant differences in MSHQ-EjD function at 1 month (UroLift change from 10.6 to 12.3 and TURP 8.6 to 7.7, p = 0.03), 3 months (UroLift 10.**8** to 11.5 and TURP 9.3 to 6.3, p = 0.0002), 6 months (UroLift 10.8 to 11.9 and TURP 8.9 to 5.7, p <0.0001) and 12 months (UroLift 10.6 to 11.9 and TURP 9.3 to 5.6, p <0.0001). No significant differences for MSHQ-EjD bother at 1, 6 and 12 months. Significant differences at 3 months (UroLift 1.7 to 1.1 and TURP 1.9 to 2.1, p = 0.01). MSHQ-EjD change was 8.9% (p=0.0129) and MSHQ-EjD Bother change was -27.4% (p=0.0002) from baseline to 3 years.	Corrected according to the published paper All listed in Table 3b. In the current document incontinence outcomes reside in this column.	Have added 3-year data for these measures but they are not comparing with TURP so have not reported this. I'm not sure where these figures are from. Anything previous to three years was included in the previous assessment report.

Issue 26

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response

Page 31 of 96. **Sonksen et al (2015).** Incontinence ISI column: In the TURP group…	Details should read: In the TURP group, patients experienced a significant worsening at both 2 weeks and 3 months. No values given. Continence preservation was comparable between the groups, and no patient experienced new-onset stress or sphincter incontinence. Of the participants who failed the BPH6 continence element (six PUL and eight TURP patients had ISI > 4 at any time), none of the PUL patients reported new-onset pad use, whereas 6 TURP patients (6/8, 75%) reported that they required pads after TURP (superior PUL performance, p = 0.01).	Corrected according to the published paper.	Changes made

Issue 27

Description of factual inaccuracy	**Description of proposed amendment**	**Justification for amendment**	**EAC response**

Page 31 of 96. Sonksen et al (2015). IPSS column: No significant differences in change in SHIM score from baseline UroLift and TURP at any of the follow-up time points. ….	Details should read: No significant differences between UroLift and TURP at 2 weeks, 1, 3 and 6 months. At 12 month follow-up, UroLift symptom improvement (**11.4**) was significantly different than TURP (**15.4**), p=0.02	Corrected according to the published paper. In the current document sexual function outcomes reside in this column.	Changes made

Issue 28

Description of factual inaccuracy	**Description of proposed amendment**	**Justification for amendment**	**EAC response**
Page 31 of 96. Sonksen et al (2015). Maximum urinary flow rate and PVR column: No significant differences between UroLift and TURP at 2 weeks, 1, 3 and 6 months…..	Details should read: Significant differences in change from baseline in Qmax at 3 months (UroLift change from 9.4 to 13.6 and TURP 9.2 to 22.6, p <0.0001), 6 months (UroLift 9.6 to 13.5 and TURP 9.4 to 19.0, p=0.003) and 12 months (UroLift 9.6 to 13.6 and TURP 9.5 to 23.2, p <0.0001). Significant differences in change from baseline in PVR at 3 months (UroLift change from 87.6 to 77.3 and TURP 98.6 to 47.6, p=0.002), 6 months (UroLift 85.5 to 80.7 and TURP 100.5 to 46.2, p = 0.003) and 12 months (UroLift	Corrected according to the published paper. In the current document IPSS outcomes reside in this column.	Changes made

	86.3 to 93.7 and TURP 103.5 to 33.6, p = 0.002).		

Issue 29

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 31 of 96. Sonksen et al (2015). IPSS-Quality of life (QoL) column: Significant differences in change from baseline in Qmax at 3 months …..	Details should read: No significant differences between UroLift and TURP at any of the follow-up time points	Corrected according to the published paper. In the current document Qmax and PVR results reside in this column.	Changes made

Issue 30

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response

Page 32 of 96. Sonksen et al (2015). IPSS: Significant differences in MSHQ-EjD function at 1 month (UroLift change from 10.6 to 12.3 and TURP 8.6 to 7.7, p = 0.03), 3 months (UroLift 10.3 ….	10.3 should read 10.8	Corrected according to the published paper	Changes made

Issue 31

Description of factual inaccuracy	**Description of proposed amendment**	**Justification for amendment**	**EAC response**
Page 34 of 96. Gratzke et al (2016). Incontinence: No figures or p-values were given.	Please see Figure 2 in the published paper. ISI for UroLift remained consistent starting at about 1.0 at baseline and varying +/-0.25 throughout follow up (not significant). For TURP, patients experienced a significant worsening at 2 weeks and 3 months, changing from about 1.25 at baseline to about 2.1 at 2 weeks (statistically significant) and 2.5 at 3 months (statistically significant).	Corrected according to the published paper	This is not part of the 2-year follow-up reported by Gratze and has therefore already been reported from Sonksen paper as part of the 1-year follow-up. No changes made.

Issue 32

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 37 of 96. Bardoli et al (2017). Erectile and sexual dysfunction	Add: No sexual dysfunction side-effects reported	Corrected according to the published paper	The proposed amendment is slightly ambiguous as it seems to relate more to adverse events. No changes made.

Issue 33

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 37 of 96. Roehrborn et al (2017). Erectile and sexual dysfunction	There was no significant degradation in mean erectile function (IIEF-5) or ejaculatory function (MSHQ-EjD Function) over the course of 5 years. Bother due to ejaculatory function improved rapidly and remained modestly improved at 5 years, p=0.02.	Corrected according to the published paper. See Table 3 in paper for details.	The EAC was reporting only ITT results. This may need to be followed up with a statistician to see if both ITT and PP analyses should be included.

Issue 34

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 37 of 96. Sievert et al (2018). Erectile and sexual dysfunction	Sexual function including ejaculation was unchanged or even improved with those who reported sexual activity prior to surgery.	Corrected according to the published paper.	Reluctant to include this as a result as this outcome is not mentioned in the methods or which measure they used. No changes made.

Issue 35

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 39 of 96. Eure et al (2019). IPSS: Significant decrease in IPSS scores between baseline and 1 month (change from 19.3 to 10.7), 3 months (19.1 to 10.4), 6 months (21.1 to 10.4), ….	21.1 should read 19.1	Corrected according to the published paper.	Changes made

Issue 36

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 41 of 96. Section 6 The severity of adverse events for this device are low with most events being Grade I or II including incontinence, erectile dysfunction and hematuria.	Please consider: The severity of adverse events for this device are low with most events being Grade I or II including hematuria and irritative symptoms, pain or discomfort. Please remove 'erectile dysfunction' and consider removing incontinence.	In the BPH6 (Sonksen et al.2015) randomised controlled trial, table 6 shows that the majority of adverse events experienced by subjects randomised to UroLift treatment experienced hematuria, irritative symptoms, pain or discomfort. UroLift patients did not experience erectile dysfunction (ED). ED was only reported for subjects randomized to TURP. The current wording suggests UroLift patients experience ED, which is not accurate. Furthermore, only one UroLift subject experience urinary incontinence, a very low rate. Within the current document, to begin	Have removed ED from paragraph and stated clearly only 1 case of incontinence

		this section with incontinence is perhaps a bit misleading.	

Issue 37

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 41 of 96. Section 6 However, one study did report several Grade IIIb events; urethral strictures, severe bleeding and secondary treatments. Nothing above a Grade IIIb (i.e. severe) was reported.	Please consider: However, one study did report several Grade IIIb events; severe bleeding and secondary treatments for LUTS. Nothing above a Grade IIIb (i.e. severe) was reported. Please remove reference to urethral stricture in this context	The inclusion of urethral stricture here is inaccurate in regards to UroLift. From BPH6 (Sonksen et al. 2015): - no UroLift subjects experienced stricture; 1 TURP patient experience stricture - The majority of secondary treatments for both UroLift and TURP patients was due to the return of LUTS, i.e. retreatment utilising either TURP, laser, PUL or Botox	Have removed urethral stricture.

Issue 38

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 41 of 96. Section 6 Failure to deliver a capsular tab may result in a delay in completing a treatment or an inability to complete a treatment for the patient.	Please add 'This failure mode, which is likely due to improper deployment as a result of user error, is outlined in the Instructions for Use (IFU) that includes proper deployment technique and positioning guidelines'	In the majority of cases there is no harm to the patient, and the procedures could be finished successfully by using another UroLift Delivery Device. This failure mode is outlined in the Instructions for Use (IFU), which includes proper deployment technique and positioning guidelines	Changes made

Issue 39

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 42 of 96. Roehrborn (2015): Grade I. …, and urge insentience.	Change insentience to incontinence	Corrected according to the published paper.	Changes made

Issue 40

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 42 of 96. Roehrborn (2015): Grade II Not reported	Detailed adverse events are listed in the L.I.F.T. Study 1 year paper (Roehrborn, J Urol 2013; 190(6): 2161-7). In addition to the mild-moderate AEs listed in the Grade I column of this document, two serious AEs were adjudicated as related to the procedure. The first was an overnight stay for clot retention coincident with reinitiating warfarin therapy, and the second was a subject who required removal of a bladder stone at 12 months that had formed from confirmed bladder gravel at	Corrected according to the published paper.	Roehrborn 2013 will not be reported within this update as it was included in the original assessment report.

	baseline and not associated with the implant.		

Issue 41

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 43 of 96. Gratzke (2017): Grades I-V: Not reported.	Detailed AEs are listed in the 1 year report of this study (Sonksen 2015).	Corrected according to the published paper.	These are already reported for the Sonksen 1-year follow-up paper. To report them again for the 2-year follow-up appear will be duplication of results.

Issue 42

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 43 of 96. Roehrborn (2017). Grade I: • UroLift: Hematuria n=1 • Urinary urge incontinence: UroLift n=1	There was only 1 subject with 1 related AE between months 49-60 per Table 1.	Corrected according to the published paper.	37-60 months need to be reported here which includes 2. However, results are very unclear as to which adverse events actually occurred.

Issue 43

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 43 of 96. Eure (2019). Grade I:	Should read 36.4%	Corrected according to the published paper.	Data reported is unreliable as only 59/100 office related AEs are

66.8%			reported and 355/353 (not a typo, 2 more than stated total) other cohort AEs are reported. Agree with % change.

Issue 44

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 44 of 96. Rubio (2019). Grade I: n=2 (10%)	Should read n=1 (5%)	Corrected according to the published paper.	Changes made

Issue 45

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 45 of 96. NHS Fife (2020)* NICE SLCS. Grade I: • Urinary urgency: n=6	Should read 'Temporary urinary urgency'	Corrected according to the published paper.	Changes made

Issue 46

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 45 of 96. NHS Fife (2020)* NICE SLCS. Grade II: UTI: n=2	Should read 'Mild UTI'	Corrected according to the published paper.	Changes made

Issue 47

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 46 of 96. Section 7: The IIEF and SHIM questionnaires, (a shortened version of the IIEF) both focus specifically on erectile dysfunction. UroLift patients did not show significant improvements in these measures over time (Bozkurt et al; 2016, Rukstalis et al; 2016 and Rubio et al; 2019).	Include relevant outcomes from the LIFT study which showed significant improvement in ED and EjD.	The LIFT pivotal study (Roehrborn et al. 2017) did show patients experienced significant improvement in ED and EjD at various timepoints post-treatment. This study is of high quality and the outcomes should be noted here	Changes made

Issue 48

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 48 of 96.	Remove QoL from this statement	The BPH6 study (Sonksen et al. 2015) demonstrated that certain elements beyond	No changes made as the QoL measure used did not show this.

In conclusion, the results are mixed and do not show that UroLift is superior when compared to TURP for urological, QoL or symptom severity outcomes.		IPSS Q8 that are representative of a better patient experience and quality of life experience (such as quicker recovery and less permanent adverse events or secondary complications) were superior for PUL compared to TURP. The clinical summary (section 9) also reinforces that less adverse events occur following UroLift compared to. TURP.	

Additions to AR:

Table 11 summaries the setting, number of participants, length of stay and theatre time for Urolift each of the studies included, and the NICE shared learning case studies for NHS implementation. It should be noted that none of the studies gave a clear definition for procedure time and there is likely to be a difference between procedure time and anaesthesia time as shown in Bardoli et al (2017). These results have been previously presented in the clinical section (tables 3,4 and 7), including additional information for comparators where available.

Table 11 Length of stay and procedure time for Urolift

Study	Setting	N Urolift	Length of stay (days)	Procedure time (minutes)
Roehrborm et al (2015) L.I.F.T study	USA Canada Australia	140	0.19	66.16 procedure time.
Sonksen (2015) The BPH6 study.	Denmark UK Germany Italy	45	1	55 minutes Anaesthesia time
Bozkurt (2016)	Turkey	17	<1 day	29.1 minutes operation time.
Gratzke et al (2016)	Germany	45	Not reported	Not reported

The BPH6 study.	UK Denmark			
Rukstalis et al (2016) L.I.F.T study	USA Canada Australia	51	0.21 days	51.25 Anaesthesia time
Bardoli et al (2017)	UK	11	10.6 hours (0.44 days)	8.5 minutes operation time. 18.7 minutes theatre time
Roehrborm et al (2017) L.I.F.T study			Not reported	Not reported
Eure et al (2019)	USA Australia	1413	Not reported	Not reported
Sievert et al (2019)	Germany	86	2.0 days	57 minutes operation time
Rubio et al (2019)	Spain	20	4.5 hours (0.1875 days)	12 minutes operative time.
Tutrone and Schiff (2020)	USA	53	Not reported	Not reported
NHS Norfolk and Norwich (2019)	UK	322	3-4 hours (0.125 – 0.167 days)	25 minutes
Northampton NHS	UK	20	0,27 days	20.11 minutes operating time
Frimley Park NHS	UK	75	Day case	25 minutes
St Helens and Knowsley Teaching Hospital NHS Trust	UK		Day case	10-30 minutes (excluding 35 minutes induction and recovery time)

NICE National Institute for Health and Care Excellence

Additional changes to the EAC report not identified in fact check responses

1. Report identified by company (22/9/20) included in page 57:

The National Day Surgery Delivery Pack (Getting it right first time, 2020) identifies Urolift as being one of a number of procedures where the focus should be to develop an outpatient rather than day surgery pathway:

2. Additional NICE shared learning case studies identified and included in table 7:

NHS Northampton January 2020	Retrospective comparison of Urolift,(n=20)_ and for TURP (n=20)	• Clinical results not reported • Operating time reduced from 45.3 min for TURP to 20.11 for Urolift • Length of inpatient stay reduced from 2.1 days for TURP to 0.27 days for Urolift.
NHS St Helens and Knowsley (2016)	Limited study details Urolift (n=7) biTURP (n=75) mTURP (n=17) HoLEP (n=6) TUIP (n=5)	• Clinical results not reported • Average length of stay for Urolift was day case and 1-2 days for all comparators • Estimated theatre time excluding 35 minutes induction and recovery (for all) was 10-30 minutes for Urolift, 30-75 minutes for biTURP, 30-60 minutes for mTURP, 60-120 minutes for HoLEP and 20-30 mintues for TUIP.
NHS Frimley park (2016)	Limited study details Urolift (n=75) TURis (n=190) Greenlight (n=80-90)	• Clinical results not reported • Urolift and Greenlight were carried out as day cases, TURis was carried out as inpatient. • Estimated theatre time was 25 minutes for Urolift, 60 minutes for TURis and Greenlight

3. Corrections to table 15 p77:

Theatre time Urolift	10 - 30		NA	16.70	Urolift cost saving if LOS < threshold
LOS Rezum	0.1-0.5		NA	0.374	Rezum cost saving if LOS ≤ threshold
LOS Urolift	0.1-0.5		NA	0.248	Urolift cost saving if LOS ≤ threshold
Cost of follow up consultation, Urolift	15.7 - 110		NA	£87.09	Urolift cost saving if followup <threshold. This is less than cost for other procedures.