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REVIEW ARTICLE

The Urolift System for the Treatment of Lower Urinary Tract Symptoms Secondary to Benign Prostatic Hyperplasia: A NICE Medical Technology Guidance

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Abstract As part of its Medical Technologies Evaluation Programme (MTEP), the National Institute for Health and Care Excellence (NICE) invited Neotract (manufacturer) to submit clinical and economic evidence for their prostatic urethral lift device, Urolift, for the relief of lower urinary tract symptoms secondary to benign prostatic hyperplasia (LUTS BPH). The Urolift System uses implants to retract the prostatic lobe away from the urethral lumen. The clinical evidence used in the manufacturer's submission shows that Urolift is effective for the treatment of BPH. Urolift delivers a weighted mean International Prostate Symptom Score (IPSS) improvement of between 9.22 and 11.82 points. These Urolift improvements are greater than a published 'marked improvement' in IPSS score of 8.80. Comparison with randomised controlled trials (RCTs) of TURP (Transurethral Resection of Prostate) and HoLEP (Holmium Laser Enucleation of Prostate) show that Urolift does not yield better clinical outcomes from baseline compared to TURP and HoLEP in terms of IPSS, QoL (Quality of Life) and Qmax (maximum urinary flow). However, Urolift appears to have the advantage in terms of minimal and mild complications, and this may be of interest to patients and urologists. The economic case for Urolift was made using a very detailed and thorough de novo cost model. The base case posed by the manufacturer placed Urolift at almost cost-neutral (£3 cost incurring, based on 2014 prices) compared to TURP, and £418 cost incurring compared to HoLEP. In an additional scenario comparing day-case Urolift with in-patient TURP, the estimated per-patient savings with Urolift were £286 compared with monopolar TURP (mTURP) and £159 compared with bipolar TURP (BiTURP). NICE guidance MTG26 recommends that the case for adoption of Urolift was supported by the evidence, when implemented in a day-case setting.

Key Points for Decision Makers

Urolift provides significant improvement from baseline in IPSS, QoL and BPHII scores but this is less than the corresponding improvement from standard treatments.

Urolift does not negatively impact erectile or ejaculatory function, and the evidence shows slight (but not statistically significant) improvements in these metrics.

Scenarios are presented in which Urolift performed as a day-case can be cost-saving compared to inpatient TURP, but not inpatient HoLEP.

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1 Introduction

This paper belongs to a series in Applied Health Economics and Health Policy summarising guidance produced by the National Institute for Health and Care Excellence

(NICE) Medical Technologies Evaluation Programme (MTEP) [1]. The programme provides guidance on medical devices and diagnostic technologies to the UK National Health Service (NHS) and supports adoption of technologies that improve clinical outcomes and patient experience, or provide a cost-saving. The MTEP process is explained in the first publication, introducing this series of papers [2]. The paper summarises the External Assessment Centre (EAC) report and how it was used to inform the NICE medical technology guidance on Urolift system for the treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia (MTG26). Cedar, the EAC for this assessment, is a collaboration between Cardiff and Vale University Health Board, Cardiff University and Swansea University. Neotract, the manufacturer of the Urolift system, notified the technology to NICE.

2 Background

2.1 Benign Prostatic Enlargement and Lower Urinary Tract Symptoms

The current NICE clinical guidelines on lower urinary tract symptoms (LUTS) (NICE CG97) define the condition as storage, voiding and post-micturition symptoms affecting the lower urinary tract [3]. In men, the most common cause of this condition is benign prostatic hyperplasia (BPH), which can occur in up to 30 % of men over the age of 65 years. Typically, first course of treatment is conservative management. If this is inappropriate or unsuccessful, drugs such as 5-α-reductase inhibitors, α-blockers and anticholinergics can be used.

NICE recommends that surgery should only be offered in cases of severe LUTS or if drug treatment has not been sufficient or appropriate. Clinicians should also inform patients that surgery effectiveness, side effects and long-term risks are uncertain [3].

The most common form of surgery is monopolar or bipolar transurethral resection of the prostate (mTURP or BiTURP), which uses transurethral electrosurgery to remove prostate tissue, during irrigation. NICE also recommend holmium laser enucleation of the prostate (HoLEP), in specialist centres or where mentorships are in place [3].

2.2 NICE Scope

2.2.1 Population

Men with LUTS secondary to BPH aged 50 or over, and with prostate volumes no greater than 100 cc (100 g). Subgroups to be considered included younger men, concerned about preservation of sexual function, or people for whom blood loss or blood transfusion may be an issue in standard surgeries, e.g. Jehovah's Witnesses.

2.2.2 Intervention

The Urolift procedure (also known as PUL, Prostatic Urethral Lift) 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 towards the prostatic capsule. A needle is used to deploy the implant, with one end of the implant 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 [4].

2.2.3 Comparators

The comparators for this technology are TURP (mTURP or biTURP) and HoLEP. These are recommended as standard surgeries by NICE CG97, with HoLEP specifically requiring a centre specialising in the technique, with mentoring arrangements in place [3]. Both TURP and HoLEP are performed under general anaesthetic, and are done transurethrally, with TURP utilising electrosurgery with fluid irrigation to remove excess prostate tissue. mTURP uses glycine as an irrigation fluid. BiTURP uses a saline solution, with the return electrode at the operation site, rather than being placed externally on the patient's thigh. Recent NICE Guidance recommends the TURiS (Olympus) biTURP system, as it has a no risk of hyponatremia (TUR syndrome, a risk of mTURP) and lower incidence of blood transfusions [5].

HoLEP uses a holmium laser rather than electrosurgery, and is performed with a modified continuous-flow resectoscope that has a circular fibre guide in the tip of the scope. An end-firing laser fibre is used to resect large pieces of prostate, which are then passed into the bladder where they are cut into smaller pieces by a morcellator, before removal [6].

The benefits to patients claimed by the manufacturer [7] were:

- Reduction in diminished ejaculatory or sexual function
- Reduced need for postoperative 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 manufacturer [7] compared with standard care were:

- 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 compared to 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 the Urolift system in men who would not otherwise consider surgical treatment

3 Review of Clinical and Economic Evidence

The manufacturer did not perform a de novo clinical data submission and synthesis. In place of this, they submitted a recent, peer-reviewed systematic review publication [8]. All results can be seen in the Perera et al. [8] manuscript and will not be reproduced in this article. However, the EAC findings are generally supportive of, and in accordance with, those in the systematic review.

3.1 External Assessment Centre (EAC) Clinical Data Synthesis

An independent literature search, performed by the EAC, did not identify any new published clinical studies on the Urolift device. We excluded a single study by Delongchamps et al. [9] as it was a non-English language publication with only four patients and was not deemed pivotal. We included the Abad et al. study [10] (professionally translated by Languages For Business Ltd., Cardiff), which was originally excluded by Perera et al. [8], as it lacked standard deviations (SDs). The EAC data synthesis was able to include data lacking SDs. All included studies in the EAC analysis are listed in Table 1.

The EAC combined results from the following studies, as they reported different aspects of the same series of patients:

1. Chin et al. [11] and Woo et al. [12] reported urological and sexual function outcomes, respectively, from the same case series.
2. Roerhborn et al. [13, 14] and McVary [15] all report on the LIFT study.

At the time of this literature search, there were no studies comparing Urolift with either TURP or HoLEP. In order to provide some comparative context for the NICE Medical Technologies Advisory Committee (MTAC) (and more fully comply with the scope for this assessment), the EAC performed a rapid pragmatic data synthesis.

The EAC's solution was to find a TURP versus 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. [17]; because it was a very recent systematic review (July 2014) and it is listed on the PROSPERO website at The University of York Centre for Reviews and Dissemination (CRD) [18]. The EAC took the publications in the systematic review and updated them where possible (and where reported results allowed). The studies are listed in Table 2.

Table 3 shows the baseline comparisons between these studies and those identified for Urolift. 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.

Data from all the published studies (Urolift and the TURP/HoLEP RCTs) were extracted by one EAC researcher and independently checked by a second. Table 4 shows each outcome measure, with the minimal clinically significant differences in each. This is sourced from publications where available, but in the absence of this, the EAC also consulted Expert Advisers. Weighted mean changes from baseline in each outcome measure are reported. We used this method of presentation to retain the original units of each outcome measure for clarity.

In order to provide the NICE advisory 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 Expert Advisers were surveyed by the EAC for their opinion on the minimum clinically significant differences in each outcome reported.

The pragmatic indirect comparison suggests the following: From similar baseline scores, both TURP and HoLEP give much better improvement in the IPSS score (including QoL, as these scores are linked) at all timepoints, with Urolift giving an improvement of −9.22 to −11.82, TURP providing −17.34 to −19.70 and HoLEP −17.68 to −20.88. BPHII scores are not reported in the TURP and HoLEP studies, but as a prostate symptom

Table 1 All included studies in the External Assessment Centre (EAC) analysis

Study	Country	Study description	Sample size
Abad et al. [10] (excluded by Manufacturer)	Spain	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 Q_{max} at 4 weeks and 3, 6 and 12 months	20
Cantwell et al. [16]	USA, Canada and Australia 19-centre study	Before and after study to assess Urolift in patients who had previously been randomly allocated 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 Primary endpoints: Symptom scores, QoL and sexual health questionnaire scores Follow-up: IPSS, IPSS QoL and BPHII were assessed at 2 weeks and 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. Q_{max} and PVR assessed at 3 and 12 months	53 (patients elected to have PUL after sham in the LIFT study)
Chin et al. [11] and Woo et al. 2012 [12]	Australia 6-centre study	Multicentre uncontrolled before and after study Primary endpoints: longer-term effectiveness of PUL in relieving LUTS [11] and effect of PUL on erectile and ejaculatory function [12] Follow-up: 2 weeks and 3, 6, 12 and 24 months	64
The LIFT study Roehrborn et al. [13, 14], and McVary et al. [15]	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 Roehrborn et al. 2013 reports 12-month urological function results [13], Roerhborn et al. 2015 is a 2-year follow-up report [14] (not included by Perera et al. [8], but included by the EAC as a long-term study) and McVary reports sexual health outcomes for the initial 12-month follow-up on the LIFT study [15] Follow-up: IPSS, QoL, BPHII, IIEF and MSHQ-EjD assessed at 2 weeks and 1, 3, 6, 12 and 24 months	Urolift group: 140 Control group: 66
McNicholas et al. [22]	7 centres in 5 countries (countries not clearly stated)	Retrospective analysis of prospectively accrued data from consecutive multicentre uncontrolled before and after study Primary endpoints: evaluate safety and efficacy with the Urolift device and surgical technique in day-to-day practice Follow-up: 2 and 6 weeks and 3, 6 and 12 months	102
Shore et al. [23]	Not reported	Uncontrolled before and after study Primary endpoint: ascertain whether 80 % of patients achieve a score of $\geq$80 on the Quality of Recovery Visual Analogue Scale (QoR VAS) by 1-month follow-up Follow-up: 2 weeks and 1 month	51
Woo et al. [24]	Australia	Prospective, non-randomised, uncontrolled before and after study 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 and 3, 6 and 12 months	19

IPSS International Prostate Symptom Score, *BPHII* Benign Prostatic Hyperplasia Impact Index, Q_{max} maximum urinary flow rate, *PUL* Prostatic Urethral Lift, *IIEF-5* International Index of Erectile Function (5-item), *MSHQ* Male Sexual Health Questionnaire, *EjD* ejaculatory domain of MSHQ, *LUTS* lower urinary tract symptoms, *RCT* randomised controlled trial, *QoR VAS* Quality of Recovery Visual Analogue Scale

Table 2 Notes on Transurethral Resection of Prostate (TURP) versus Holmium Laser Enucleation of Prostate (HoLEP) randomised controlled trial (RCT) studies identified by Li et al. [17]

Study	Notes
Ahyai et al. [19]	Replaces Kuntz et al. [20], as this contains 2-year follow-up results
Eltabey et al. [21]	
Gilling et al. [22]	4-year results published, but not usable—dropout rates not reported for each patient group
Gupta et al. [23]	
Mavuduru et al. [24]	Only reports results up to 9 months post-procedure
Montorsi et al. [25]	
Sun et al. [26]	
Tan et al. [27]	2-year and 7-year results published, but not usable – dropout rates not reported for each patient group

Table 3 Baselines comparison between Urolift studies and Transurethral Resection of Prostate (TURP) versus Holmium Laser Enucleation of Prostate (HoLEP) randomised controlled trials (RCTs) from Li et al. [17]—data expressed in ranges

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 (ml)	41.3–51	36.5–77.8
Q_{max} (ml/s)	6.9–8.85	4.9–8.9

IPSS International Prostate Symptom Score, Q_{max} maximum urinary flow rate

score, it should give general improvements in agreement with IPSS scores.

Q_{max} improvements are higher at all time points for both TURP and HoLEP, with Urolift giving a +3.53 to +4.16 ml/s improvement from baseline. TURP provides a +14.11 to +23.20 ml/s improvement, and HoLEP +15.29 to +23.10 ml/s.

TURP and HoLEP 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 Expert Adviser questioned the importance of PVR as an outcome measure for Urolift, and presumably other surgical treatments for BPH. This validity of PVR as a reliable outcome measure is also questioned in NICE CG97 [3].

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 Expert Adviser recommended the GOLIATH study for more reliable 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 [29]. Another Expert Adviser recommended the 6-year follow-up on HoLEP by Gilling et al. [30] for sexual function post-HoLEP; and a 76 % retrograde ejaculation rate is reported, which was confirmed by surveying our clinical advisers (estimates ranged from 70–80 %). IIEF improvement from baseline was not reported.

Complications reported should also be interpreted cautiously and in the knowledge that there are no truly 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 versus HoLEP RCTs, and with good reason: Urolift complications seem to be typically mild, such as transient dysuria or haematuria. Presumably, dysuria and haematuria are mild, yet expected, occurrences with TURP and HoLEP.

3.2 Manufacturer's Economic Submission

No published economic studies of Urolift were identified by the manufacturer or the EAC, in independent literature searches.

The manufacturer presented comprehensive de novo economic model for their economic submission. The manufacturer's de novo model structure is a decision tree, with seven executable arms, one for each technology or comparator. Only four of these are relevant to this assessment according to the scope: Urolift, mTURP, BiTURP and HoLEP. The sponsor's submission was from the NHS and personal social services perspective and presents a 2-year time horizon.

Following treatment, the outcomes are success or failure. Success is defined as ">10 % improvement in IPSS within 12 months", and the probability with each in-scope treatment is: Urolift: 89.80 %, mTURP: 94.00 %, HoLEP: 96.71 % and biTURP: 94.0 %. The success category then has options for relapse or no relapse: Urolift: 0.00 %, mTURP: 0.17 %, HoLEP: 0.32 % and biTURP: 0.99 %. 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.

The model includes costing for the following complications: Incontinence, urinary retention, urinary tract infection (UTI), stricture, TUR syndrome, decrease in erectile function, increase in erectile function and ejaculation dysfunction.

The base case assigned a cost of £2342 per patient for Urolift (based on 2014 prices). This was slightly cost incurring, by £3, compared to monopolar TURP (£2339 per

Table 4 Overview of Urolift, TURP and HoLEP results

	Published or Expert Adviser opinion – minimally important change	Urolift	TURP	HoLEP
IPSS	Minimum = 3.0	1 month − 10.35	1 month − 17.34	1 month − 17.68
(Negative score is improvement)	Moderate = 5.1	3 months − 11.82	3 months − 19.70	3 months − 20.88
	Marked change = 8.8	12 months − 10.49	12 months − 18.13	12 months − 19.29
	[28]	24 months − 9.22	24 month − 17.50	24 months − 20.40
IPSS QoL	Minimum = 1–3	1 month − 2.27	1 month − 2.99	1 month − 2.64
(Negative score is improvement)	(Expert Adviser opinion)	3 months − 2.48	3 months − 2.80	3 months − 3.00
		12 months − 2.31	12 months − 3.18	12 months − 3.24
		24 months − 2.22	24 months N/A	24 months N/A
BPHII	Minimum = 0.5 Moderate = 1.1	1 month − 3.29	N/A	N/A
(Negative score is improvement)	Marked changed = 2.2	3 months − 3.96		
	[28]	12 months − 3.95		
		24 months − 3.76		
IIEF	Minimum = 4	1 month + 0.52	N/A	N/A
(Positive score is improvement)	(Expert Adviser opinion)	3 months + 1.34		
		12 months + 0.80		
		24 months N/A		
MSHQ-EjD	Minimum = 1.5	1 month + 1.82	N/A	N/A
(Negative score is improvement)	(Expert Adviser opinion)	3 months + 1.47		
		12 months + 0.83		
		24 months N/A		
MSHQ-Bother	Minimum = 1.0	1 month − 0.67	N/A	N/A
(Negative score is improvement)	(Expert Adviser opinion)	3 months − 0.79		
		12 months − 0.91		
		24 months N/A		
Q_{max} (ml/s)	Minimum = 2ml/s	1 month + 4.16	1 month + 14.58	1 month + 15.29
(Positive is improvement)	[3]	3 months + 3.78	3 months + 14.11	3 months + 18.25
		12 months + 3.52	12 months + 16.69	12 months + 17.78
		24 months + 4.15	24 months + 3.20	24 month + 23.10
PVR (ml)	Minimum = 50 ml	1 month − 7.00	1 month − 137.43	1 month − 160.23
(Negative is improvement)	(Expert Adviser opinion)	3 months − 10.34	3 months − 89.34	3 months − 78.00
		12 months − 5.72	12 months − 127.29	12 months − 161.47
		24 months N/A	24 months − 196.10	24 months − 231.40

IPSS International Prostate Symptom Score, *BPHII* Benign Prostatic Hyperplasia Impact Index, Q_{max} maximum urinary flow rate, *PUL* Prostatic Urethral Lift, *IIEF* International Index of Erectile Function, *MSHQ* Male Sexual Health Questionnaire, *EjD* ejaculatory domain of MSHQ, *LUTS* Lower Urinary Tract Symptoms, *QoL* quality of life, *PVR* Post-Void Residual Volume, *TURP* Transurethral Resection of the Prostate, *HoLEP* Holmium Laser Enucleation of the Prostate

patient), by £38 compared to bipolar TURP (£2302) and by £418 compared to HoLEP (£1924 per patient). These figures are shown in Table 5 alongside the EAC's sensitivity analysis and input testing.

The key drivers of the model are the number of Urolift implants used, operating time and length of stay.

3.2.1 Critique of the Manufacturer's Economic Model

The EAC found many of the manufacturer's economic inputs to be appropriate and backed by published sources. The Urolift data were taken from the LIFT study [13–15] and Chin et al. [11]. Comparator data were taken from a health technology assessment (HTA) by Lourenco et al. [31].

The manufacturer's inputs for post-Urolift length of stay (0.5 days) and procedure time (30 min) were based on the clinical opinion of three experts. A weighted mean procedure time of 59.6 min was calculated from the Urolift publications, but we were assured by Expert Advisers that this was 'trial conditions', and 30 min was a more appropriate input.

Table 5 External Assessment Centre (EAC) input testing and sensitivity analysis—bold type indicates where Urolift is cost saving or cost neutral

Model input	Values (sponsor's base case input in brackets)	Urolift	mTURP (incremental cost of Urolift in brackets)	HoLEP (incremental cost of Urolift in brackets)	biTURP (incremental cost of Urolift in brackets)
BASE CASE		£2342	£2339	£1924	£2302
			(+£3)	(+£418)	(+£40)
Number of Urolift implants	4.4	£2474	£2339	£1924	£2302
	(4)		(+£135)	(+£550)	(+£172)
Urolift operative time (mins)	60	£2496	£2339	£1924	£2302
	(30)		(+£157)	(+£572)	(+£194)
Urolift length of stay (days)	0.25	£2256	£2339	£1924	£2302
	(0.5)		(+£83)	(+£332)	(+£46)
	1	£2514	£2339	£1924	£2302
	(0.5)		(+£175)	(+£590)	(+£212)
mTURP operative time	66	£2345	**£2371**	£1924	£2302
	(60)		(***−£26***)	(+£421)	(+£43)
Theatre overheads	£5.23 per min	£2532	**£2671**	£2372	**£2611**
	(not included by manufacturer, added by EAC)		(***−£139***)	(+£160)	(***−£79***)
Band 5 nurse (TURP fluid handling)	2 band 5 nurses for TURP	£2351	**£2429**	£1924	**£2385**
	(1 band 5 nurse)		(***−£78***)	(+£427)	(***−£34***)
Cost of transfusion	£329	£2338	£2294	£1913	£2255
	(£862.17)		(+£44)	(+£425)	(+£83)
Cost of mTURP and biTURP capital equipment	£10	£2343	**£2349**	£1924	£2312
	(£0)		(***−£6***)	(+£419)	(+£31)
Cost of mTURP consumables	£56.84	£2343	**£2343**	£1924	£2306
	(£52.50)		(***±£0***)	(+£419)	(+£37)
HoLEP fibres	£368.61, single use	£2342	£2339	£2262	£2302
	(£614.27, 20 uses)		(+£135)	(+£80)	(+£40)
	£1207.42, 20 uses	£2342	£2339	£1954	£2302
			(+£135)	(+£388)	(+£40)
Band 5 nurse (HoLEP laser operator)	Two band 5 nurses for HoLEP	£2342	£2339	£2033	£2302
	(one band 5 nurse)		(+£135)	(+£309)	(+£40)

mTURP Monopolar Transurethral Resection of the Prostate, *biTURP* Bipolar Transurethral Resection of the Prostate, *HoLEP* Holmium Laser Enucleation of the Prostate

The number of Urolift devices is a key driver of the model. In the base case, the manufacturer has used 4 as the number of devices per procedure [11]. 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.

Blood transfusion is not likely to be required when using Urolift, based on the clinical evidence in this assessment. The manufacturer overestimated the cost of blood transfusion as £862.17 per transfusion for the comparators. This is a top-down costing based upon NICE CG97 [3, 32]. This provides a cost of £635 in 2003, inflated by the manufacturer to current value of £826.17. This also includes an additional day's length of stay. The EAC estimates the cost of blood transfusion as £329. One unit standard red cells = £121.85 [33]. The mean number of units per transfusion is estimated to be 2.7 units of red blood cells when transfusion is required [32]. Therefore the EAC calculates $2.7 \times £121.85 = £329$ per transfusion. The probability of blood transfusion for Urolift in the model is zero; therefore, this change reduces the cost of the comparators, but not Urolift.

The unit cost of hospital stay was taken from published Scottish data for urology specialty in-patient costs [34], 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 [35], minus the procedure costs included in the model. It is not clear which procedure costs were 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 × £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) [35].

3.2.2 EAC Revisions/Sensitivity Analysis of the Manufacturer's Economic Model

We performed a number of input tests and sensitivity analyses where the published evidence or expert advice did not agree with those inputs used by the manufacturer's model. For each, the single input was changed to assess its impact on the model.

As discussed in Sect. 3.2.1, the EAC substituted the manufacturer's estimate of four Urolift implants, with the weighted mean of 4.4 implants. We tested a Urolift operative time of 60 min, in line with the weighted mean procedure time from the Urolift publications. We tested an mTURP procedure time of 66 min, taken from the EAC comparator studies. We included operating theatre costs for all procedures, using the cost of a urology operating theatre from NICE CG97 [3], stated at £9 per minute. We also tested a greater post-Urolift length of stay (LOS) range, from 0.25 to 1 days.

An extra Band 5 nurse was added to the TURP procedures, as Expert Advisers stated that an additional nurse is often needed to handle irrigation fluid. The impact of an additional 'laser operator' Band 5 nurse was also tested for HoLEP.

The EAC changed the cost of blood transfusion in the model from £862.17, which includes double counting of one additional day in hospital to the EAC estimate of £329.

We included a £10 per procedure cost for capital equipment for TURP (total capital cost £20,799 used both mTURP and biTURP) as the manufacturer did not include the capital cost in the base case.

We updated the cost of TURP consumables to £56.80 to account for roller and ball electrodes and a return electrode plate (return plate for mTURP only). HoLEP fibres were tested in a single-use scenario, with a price of £368.61 for single-use HoLEP fibres. All prices were taken from the NHS Supply Chain. We were also able to perform a 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.

All of these analyses, including the manufacturer's base case, are presented in Table 5.

3.2.3 Additional scenario modelled by the EAC

Urolift can be performed as a day-case, whereas TURP is performed as an inpatient procedure – this was confirmed as a realistic UK practice by our clinical Expert Advisers. This scenario relies upon a number of specific inputs, requiring only 0.125 days (3 h) length of stay in total, a 30-min procedure time for Urolift and a 66-min procedure time for TURP. The scenario includes urological theatre overhead time and the more realistic cost of blood transfusion of £329, as mentioned in Sect. 3.2.1. The model inputs are detailed in Table 6, and the EAC Scenario cost results are shown in Table 7.

4 NICE Guidance

4.1 Preliminary Guidance

The evidence submitted by the company and the EAC's report were presented to MTAC, who produced the following draft recommendations:

Table 6 'Urolift as day case' EAC scenario inputs and conditions

Input	Conditions	Source/notes
Urolift length of stay	0.125 days (3 h)	Clinical expert advice
Urolift procedure time	30 min	Clinical expert advice/manufacturer's model
Number of Urolift implants	4[a]	Manufacturer's model
Theatre overhead cost (all procedures)	5.23 per min	Added to model as Nurse Band 5 (second)
mTURP procedure time	66 min	EAC weighted mean from clinical section of this Assessment report
Cost of blood transfusion	£329	EAC figure (manufacturer's original input was too high)

mTURP Monopolar Transurethral Resection of the Prostate

[a] 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 remains cost saving compared to mTURP and BiTURP under these conditions

Table 7 External Assessment Centre (EAC) scenario cost results

	Urolift	mTURP	HoLEP	BiTURP
Manufacturer base case	£2342	£2339	£1924	£2302
EAC scenario	£2405	£2691	£2315	£2564
Incremental cost of Urolift (negative if Urolift is cost saving)		−£286	+£90	−£159

mTURP Monopolar Transurethral Resection of the Prostate, *biTURP* Bipolar Transurethral Resection of the Prostate, *HoLEP* Holmium Laser Enucleation of the Prostate

"The clinical and cost case for adopting the Urolift system for treating symptoms of benign prostatic hyperplasia is supported by the evidence if it is used in a day surgery unit. 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). It also reduces the length of hospital stay and may be done in a day surgery unit."

"The Urolift system should be considered for use 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 cm^3."

"Cost modelling estimates that using the Urolift system in a day surgery unit results in cost savings of around £286 and £159 per patient compared with monopolar and bipolar transurethral resection of the prostate (TURP) respectively, and incurs extra costs of around £90 per patient compared with holmium laser enucleation of the prostate (HoLEP). The primary cost driver in the modelling is the unit cost, and number of implants used per treatment. For inpatient treatment it is estimated that the Urolift system becomes cost neutral if the price per implant is £268 (compared with TURP) or £281 (compared with HoLEP)."

4.2 Consultation Response

During the consultation period, NICE received 37 consultation comments from 13 consultees (six NHS professionals, four patients, two medical technology manufacturers and one professional society). The comments concerned the comparators, the costs, patient population and patient benefit. The Committee discussed the chosen comparators and heard from expert advice that HoLEP was not widely used in the UK. Because of this the Committee removed the reference to HoLEP from the recommendations. During the consultation period, NICE became aware that new results had been published for the LIFT [36] and BPH6 [37] trials. The EAC assessed this new information and concluded that it supported the assumptions made in the guidance.

5 Key Challenges and Learning Points

One issue in this assessment was the lack of evidence that genuinely fit the original scope. The scope called for studies with TURP and HoLEP as comparators, and no direct comparative studies were available at the time of writing. The EAC's pragmatic solution to find a recent, robust TURP versus HoLEP systematic review, and extract the data from the source publications is limited in its utility and cannot replace a truly comparative study on a single patient cohort.

In their economic model, the manufacturer presented Urolift at almost cost neutral versus mTURP, and cost incurring against the BiTURP and HoLEP. The EAC therefore modelled a realistic day-case scenario for Urolift, based on UK clinical expert advice, which demonstrated potential cost savings.

6 Conclusions

The evidence supports Urolift as 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 clinical rating tool [28]. However, a pragmatic indirect comparison with TURP versus HoLEP RCTs selected from a recent, high-quality systematic review [17] suggests that Urolift does not yield better clinical outcomes compared to TURP and HoLEP in terms of IPSS, QoL and Q_{max} improvements from baseline, in patients with similar baseline characteristics.

Urolift appears to have an advantage in terms of fewer and milder complications. The clinical evidence shows that Urolift is actually associated with slight, non-statistically significant improvement in sexual function. Expert Advisers 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 economic case for Urolift was made using a de novo cost model. Inputs to the model were well researched and

relied upon a robust HTA for TURP and HoLEP inputs [31], and two 2-year follow-up studies on Urolift [13–15] for the Urolift inputs.

The base case presented by the manufacturer placed Urolift at almost cost-neutral (£3 cost incurring) compared to monopolar TURP and £418 cost incurring compared to HoLEP. The key drivers of the model were the cost of the Urolift device and length of stay post-procedure.

The EAC modelled an additional scenario for Urolift as a day-case which relies upon a low number of Urolift implants, a short procedure time of 30 min or less, adding urological operating theatre overhead costs, and a day-case procedure of 0.125 days (3 h). Under these conditions, savings of £286 compared with mTURP and £159 compared with BiTURP are achievable. All of the inputs of the EAC scenario are supported by published sources or by Expert Advisers for the assessment, who are currently using the Urolift device in the UK.

One weakness of this assessment report was the lack of available directly comparative Urolift versus TURP evidence. This led the EAC to synthesise a pragmatic comparison, sourcing TURP comparator data from a recent systematic review [17]. It should be noted that there is now published evidence from the BPH-6 trial [37], which randomly allocated patients to either Urolift or TURP (the TURP is not named as monopolar or biplolar, rather 'standard local practice', and therefore may be either, or both). The conclusions of this study are that both Urolift and TURP give satisfactory improvements in symptoms and functional measurements. This agrees with the findings in the assessment report and the expert opinion on minimum clinical significance thresholds for each metric.

As shown in the EAC's pragmatic Urolift/TURP comparison, IPSS, Q_{max} and PVR improvements from baseline were greater after TURP than after Urolift. However, the BPH-6 results show that the difference between the two procedures are statistically significant, but by a smaller marginal IPSS improvement than in the pragmatic EAC comparison. For example, at 12 months, Urolift in BPH-6 delivered an average IPSS decrease of -11.4 ± 8.4 (The EAC report analysis shows an decrease of -9.22 to -11.82). The IPSS improvement after TURP was 15.4 ± 6.8 (the EAC pragmatic comparison showed this as -17.34 to -19.70).

Additionally, there are now 3-year LIFT study results available [36], which are very similar to those shown in the 1- and 2-year LIFT study publications included in this EAC report. The 3-year follow-up shows that Urolift continues to be effective 3 years post-operatively, with very mild adverse events. The results do not change significantly from those presented in 1- and 2-year follow-ups, as shown in the assessment report.

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All clinical expert advice can be found here: https://www.nice.org.uk/guidance/MTG26/documents/urolift-for-treating-lower-urinary-tract-symptoms-of-benign-prostatic-hyperplasia-clinical-expert-advice2

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