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Original Article

The cost-effectiveness of transurethral resection of the prostate vs thulium laser transurethral vaporesection of the prostate in the UNBLOCS randomised controlled trial for benign prostatic obstruction

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Trial Registration ISRCTN registry – ISRCTN00788389.

Objective

To determine the cost-effectiveness of the current 'gold standard' operation of transurethral resection of the prostate (TURP) compared to the new laser technique of thulium laser transurethral vaporesection of the prostate (ThuVARP) in men with benign prostatic obstruction (BPO) within the UK National Health Service (NHS).

Patients and Methods

The trial was conducted across seven UK centres (four university teaching hospitals and three district general hospitals). A total of 410 men aged ≥18 years presenting with either bothersome lower urinary tract symptoms (LUTS) or urinary retention secondary to BPO, and suitable for surgery, were randomised (whilst under anaesthetic) 1:1 to receive the TURP or ThuVARP procedure. Resource use in relation to the operation, initial inpatient stay, and subsequent use of NHS services was collected for 12 months from randomisation (equivalent to primary effectiveness outcome) using hospital records and patient questionnaires. Resources were valued using UK reference costs. Quality adjusted life years (QALYs) were calculated from the EuroQoL five Dimensions five Levels (EQ-5D-5L) questionnaire completed at baseline, 3- and 12-months. Total adjusted mean costs, QALYs and incremental Net Monetary Benefit statistics were calculated: cost-effectiveness acceptability curves and sensitivity analyses addressed uncertainty.

Results

The total adjusted mean secondary care cost over the 12 months in the TURP arm (£4244) was £9 (95% CI –£376, £359) lower than the ThuVARP arm (£4253). The ThuVARP operation took on average 21 min longer than TURP. The adjusted mean difference of QALYs (0.01 favouring TURP, 95% CI −0.01, 0.04) was similar between the arms. There is a 76% probability that TURP is the cost-effective option compared with ThuVARP at the £20 000 per QALY willingness to pay threshold used by National Institute for Health and Care Excellence (NICE).

Conclusion

One of the anticipated benefits of the laser surgery, reduced length of hospital stay with an associated reduction in cost, did not materialise within the study. The longer duration of the ThuVARP procedure is important to consider, both from a patient perspective in terms of increased time under anaesthetic, and from a service delivery perspective. TURP remains a highly cost-effective treatment for men with BPO.

Keywords

benign prostatic obstruction, cost-effectiveness analysis, transurethral resection of the prostate, thulium laser transurethral vaporesection of the prostate, quality of life, #Andrology

Introduction

In the UK, 25 000 men are operated on annually to relieve the symptoms caused by benign prostatic obstruction (BPO), and TURP is the most common procedure undertaken [1,2]. The small but significant mortality and morbidity risks associated with the TURP procedure including haemorrhage, transurethral resection (TUR) syndrome and UTIs [3] have led to the development of new technologies for treating men with BPO.

The UK National Institute for Health and Care Excellence (NICE) currently recommends the following interventions for men with BPO: TURP; holmium laser enucleation of the prostate (HoLEP) (in centres specialising in the technique) [4]; and GreenLight XPS laser [5] for lower risk patients. TURP remains the standard with which new techniques should be compared.

The thulium laser technique vaporises and resects the prostate, using a surgical technique similar to TURP, facilitating a shorter learning curve and potentially making it quickly generalisable. In China, a randomised controlled trial (RCT) [6] and a non-randomised prospective controlled trial [7] compared TURP and thulium laser transurethral vaporesection of the prostate (ThuVARP). This led to the European Association of Urology (EAU) guidelines on laser technologies [8] stating that ThuVARP shows equivalent efficacy to TURP. However, no trial within a recent systematic review of the two techniques reported costs, although the associated meta-analysis did find a shorter length of stay in favour of ThuVARP [9].

In the UK, the UNBLOCS multicentre, pragmatic, randomised, controlled, parallel-group trial showed that both ThuVARP and TURP were effective treatments for men with BPO, with TURP having some minor benefits compared with ThuVARP at 12 months [10].

The present article presents the within-trial individual patient data cost-effectiveness analysis of the UNBLOCS trial over a 12 month period from a secondary care UK NHS perspective and a wider NHS perspective, which includes community-based health care.

Patients and Methods

Patients and Interventions

Men in seven UK secondary care centres were invited to participate in the trial if they were aged ≥18 years and presented with either urinary retention or bothersome LUTS, secondary to BPO, and were suitable for TURP surgery. The design of the trial has been published previously [11]. In brief, men meeting the study's inclusion criteria and who gave fully informed consent were randomised, once they were anaesthetised in the operating theatre, to receive either TURP or ThuVARP in a 1:1 ratio between June 2014 to December 2016 and were followed up for 12 months post-randomisation/surgery. Participants were blinded to which procedure they received during their involvement in the trial. ThuVARP was selected for comparison rather than thulium enucleation as it easier to learn, so facilitating the opportunity for widespread adoption into clinical practice. All surgeons were familiar with laser use for procedures such as stone surgery, and some had used HoLEP/Greenlight XPS. All surgeons were trained to conduct the ThuVARP procedure before starting the trial, as published elsewhere [11]. As patients were randomised in theatre, sites made the decision on whether to list patients as daycase or inpatient procedures irrespective of their surgical arm. Ethical Approval was given by the National Research Ethics Service (NRES) Committee South Central - Hampshire B Ethics Committee (13/SC/0644).

Resource use Measurement and Valuation

Resource use data in relation to the initial surgery and any subsequent treatment for the man's BPO were collected for 12 months post-randomisation from three main sources; Trial Case Report Forms (CRFs); Hospital Patient-linked information costing systems (PLICS), and patient-completed questionnaires.

Study research nurses within the treating hospitals recorded resource use information relating to the operation and postoperative stay onto CRFs capturing items such as surgery time, use of disposable theatre equipment, complications, unscheduled returns to the operating theatre, and any time spent on different postoperative wards.

PLICS is an electronic NHS cost reporting tool which has information in the form of International Statistical Classification of Diseases (ICD)10, Office of Population Censuses and Surveys Classification of Interventions and Procedures version 4 (OPCS-4) and Health Resource Group (HRG) codes, on specific patient events related to their secondary care healthcare use. Data on subsequent inpatient stays, daycases, admissions, and outpatient visits and procedures were obtained from PLICS for six out of the seven centres. For one centre where this was not possible, all inpatient stays and outpatient visits were manually extracted from the hospital systems. We defined the secondary care NHS perspective as resource use data obtained from the CRFs and hospital systems.

A questionnaire collecting resource use data directly from participants at 3- and 12-months follow-up was either posted to or given to the men in clinic for completion at home. The questionnaires were used to collect information on

community-based healthcare use (e.g. GP visits, district nurse visits), non-treating hospital secondary care healthcare use, and medications resulting from their treatment. The NHS perspective is defined as resource use information obtained from all sources. All study data were managed using REDCap [12] hosted at the University of Bristol.

All resource use and the unit costs (2016/17 UK prices) used to value the respective resources are given in Table 1 [13–18] Information from the Hospital Trust finance department from one participating hospital was used in costing the operation and the initial hospital stay. Information from equipment manufacturers was used to cost all theatre equipment, which differed between the two procedures. UK reference costs were used to value subsequent inpatient stays, outpatient visits, and procedures and community-based healthcare [13,14].

Outcome Measurement

The economic outcome for the analysis is given in quality adjusted life years (QALYs) as recommended by NICE [19]. At baseline participants completed the five level EQ-5D (EQ-5D-5L) questionnaire in clinic, while at 3- and 12-months it was either posted to or given to the men at clinic for completion at home. At 6 weeks of follow-up the EQ-5D-5L was administered by post. The EQ-5D-5L values were transformed into utility scores [20]. QALYs for each patient were calculated from the utility scores using the area under the curve approach, taking into account any deaths that occurred during the study [21].

Missing Data

Simple imputation was used for missing data items occurring during the operation (see Table 1 for details). In relation to the missing items from the resource use questionnaires, if the questionnaire had been returned and an item was missing it was assumed that no resource had been used.

Multiple imputations by chained equations were then used. The model included: baseline, 6-weeks, 3- and 12-months utility variables, trial arm, baseline diagnosis of LUTS or urinary retention, baseline comorbidities, age, and centre. In

Table 1 Resources collected and their valuation (2016/17 prices excluding value-added tax [VAT]).

Resource	Unit cost, £	Source of cost
Theatre time	15.70/min[a]	Finance Department of a treating hospital
Recovery ward	12.71/min[b]	Finance Department of a treating hospital
Laser capital and reusable equipment[d]	93.61[c]	Manufacturer
Laser consumables[e]	Varies	Manufacturer
TURP capital and reusable equipment[f]	15.81[c]	Manufacturer
TURP consumables[g]	Varies	Manufacturer
Blood transfusion	498.26	NHS reference cost [13]
Ward	360/day	Finance Departments of a treating hospital
HDU/ITU	1300/day	Finance Departments of a treating hospital
Subsequent inpatient stays	Varies[h]	NHS reference costs [13] Curtis and Burns (2017) [14]
Day cases	Varies	NHS reference costs [13]
Outpatient visits	Varies[i]	NHS reference costs([13]
Outpatient procedures	Varies[j]	NHS reference costs [13]
Accident and emergency attendances (no admission)	147.80	NHS reference costs [13]
GP surgery visit	29[k,l]	Curtis and Burns (2017) [14]
GP home visit	89.44[k,l,m]	Curtis and Burns (2013) [15]
GP telephone call	14.60	Curtis and Burns (2017) [14]
GP nurse visit	5.53 [l,n]	Curtis and Burns (2017) [14]
District nurse visit	38.68[m]	Curtis (2015) [16]
Community continence nurse visit	83	NHS reference costs [13]
NHS 111 call	12.26	Pope et al. (2017) [17]
Community-based urology service visit	103	NHS reference costs [13]
Medication[o]	Varies	The Drug Tarriff [18]

[a]The theatre unit cost of £15.70/min is an adjusted cost to avoid double counting of equipment. This adjusted cost is allocated to initial theatre time. The unadjusted unit cost of £17/min is employed for return to theatre cases (n = 2) and for cases where neither ThuVARP, TURP or conversion procedures were carried out (n = 7). If the start of resection time was missing (n = 35), The anaesthetic start time was used. [b]If the time leaving recovery ward or discharge time (for day cases) was missing (n = 52) then a three-hour duration was used based on information given by one of the hospitals. [c]Costs are derived from the number of TURP operations performed annually in a single operating theatre (n = 260), the cost from the manufacturer and the lifespan of the equipment (in order to calculate an 'annual equivalent cost') and the annual maintenance costs [d]The laser capital and reusable equipment cost includes the laser machine, working element, cystoscope, bridge, telescope, light lead, sheath, outer sheath, visual obturator and laser goggles. [e]Laser consumables costs comprises of laser fibres, biopsy forceps and evacuator kits. If the type of laser fibre used was missing (n = 5) a reusable fibre was assumed, if number of reusable laser fibres were missing (n = 14) one was assumed. [f]TURP capital and reusable equipment costs the TURP generator, working element, telescope, light lead, inner sheath, outer rotating sheath, bipolar lead and visual obturator. [g]TURP consumables cost consist of the cost of loop electrodes, roller electrodes, biopsy forceps and evacuator kits. [h]The elective inpatient cost related to the relevant HRG was used. [i]A consultant led unit cost relating to the relevant service code (i.e. speciality) was used. [j]The unit cost relating to the Service code and relevant HRG was used. If the HRG was missing the overall unit cost for the relevant service code was used. [k]Excluding direct care staff costs [l]Excluding qualification costs [m]Hospital and Community Health Services (HCHS) index was used to inflate costs to 2016–17 prices [n]Based on the assumption of a 9.22-min consultation [o]If dosage was missing then the usual dose was used.

all, 54 individual imputations were conducted and combined using Rubin's rules [22] in relation to both perspectives using a randomisation seed to enable reproducible imputations.

Analysis

The economic analyses were conducted under an intention-to-treat approach analysing the groups as they were randomised. STATA 15.1 [23] was used for all analyses. Discounting did not occur in this study as discounting in economic evaluations only occurs if the follow-up for a study is >1 year.

The cost of each item of resource used during the 12 months of follow-up was calculated by multiplying the resource use (e.g. number of laser fibres) by its unit cost and summed by resource use category (e.g. laser consumables) for each participant.

Adjusted mean costs and QALYs by trial arm and the differences in adjusted mean costs and QALYs (and their associated 95% CIs) between trial arms were estimated using the seemingly unrelated regressions (SUR) method, which accounts for the correlation between costs and QALYs [24]. Costs and QALYs were adjusted for the randomisation stratification variables, centre and bothersome LUTS or urinary retention. Additionally, QALYs were adjusted for baseline utility.

The secondary care costs and NHS costs were compared with QALYs in turn. Within each perspective, if neither treatment was more expensive and less effective than the other, incremental cost-effectiveness ratios (ICERs) were created using SUR. The incremental Net Monetary Benefit (NMB) statistic that summarises the differences in costs and QALYs of TURP compared with ThuVARP, at the standard NICE willingness to pay threshold of £20 000 per QALY [19], was calculated using the SUR outputs. A positive statistic would indicate that TURP is the cost-effective option.

To explore sample uncertainty within the cost-effectiveness estimates, cost-effectiveness acceptability curves (CEACs) were calculated from individual NMB values at each willingness-to-pay per QALY threshold (£0 to £100 000). The CEAC shows the probability that TURP is the cost-effective option compared with ThuVARP at different willingness to pay per QALY thresholds.

The following one-way sensitivity analyses were conducted to test the robustness of different parameter estimates and assumptions made in relation to items of resource use and costs in relation to the secondary care analysis.

- A complete case analysis (i.e. including only participants with complete data, i.e. no simple or multiple imputation was used).
- The exclusion of prostate cancer-related hospital resource use.
- The application of the average times of theatre by arm and centre from the last 25% of cases to all other cases. This was conducted in order to examine whether there is a learning curve effect in the time taken to conduct the THuVARP operations, as all surgeons were trained in the technique for the purposes of the trial.
- The exclusion of post-recovery ward costs for those patients who were randomised to ThuVARP in centres where daycase TURP procedures were not conducted, to examine the cost implication of being able to conduct the ThuVARP procedure as a daycase. In the trial all patients in these centres had to be listed as inpatient procedures.
- The exclusion of the capital equipment costs (e.g. the laser and the TURP generator) from both operations to reflect the fact that often manufacturers do not charge for capital equipment provided enough consumables are purchased; adjusting the number of people that would have had the operation in a year to reflect a high use and a low use of the equipment; and the addition of TURP capital costs to those randomised to ThuVARP to account for TURP equipment needing to be available because of conversions to TURP during the trial in part due to equipment issues.
- The application of an alternative recovery time cost (£2.58/min) based on a recent surgical microcosting study [25] to acknowledge that the cost per hour of recovery based on a medi room (a room to which patients are admitted to, prepared for and recovered from surgery and discharged from, if an overnight stay is not required) may not reflect recovery costs in other institutions.

Results

A total of 410 participants were randomised in the UNBLOCS study. Resource use and cost data from the CRFs and hospital systems (the secondary care NHS perspective) were available for 385 men (95% of the 407 randomised men who did not withdraw their data). Missing data within the resource use questionnaires meant that the completeness of the resource use and cost data reduced to 47% once information from all data sources was used (the NHS perspective). The EQ-5D-5L data were complete for 89% of men at baseline; 82% at 6 weeks, 78% at 3 months and 81% at 12 months, although intermittent missingness meant that complete QALY data was only obtained for 212 participants (52%). The amount of missing data meant that the cost, QALY and SUR analyses were conducted using the multiple imputed (MI) dataset comprising all 407 randomised men (TURP n=204 and ThuVARP n=203).

The operation took on average 21 min longer in the ThuVARP arm than in the TURP arm (Table 2), whereas those in the TURP arm spent 14 min longer in recovery. Few

Table 2 Mean (SD) resource use[a] by category and randomised allocation.[b]

Resource use category (unit of resource use measurement)	TURP		ThuVARP	
	N	Resource use, mean (SD)	*N*	Resource use, mean (SD)
Theatre time, min	196	61.50 (28.57)	191	82.48 (33.57)
Recovery ward, min	196	157.58 (170.75)	191	143.97 (138.43)
Laser reusable equipment,uses,*n*	204	0	203	0.93 (0.26)
Laser consumables, *n*	204	0	202	2.23 (0.88)
TURP reusable equipment, uses, *n*	204	0.98 (0.14)	203	0.24 (0.43)
TURP consumables, *n*	204	2.54 (0.72)	203	0.42 (0.83)
Blood transfusion, units, *n*	204	0.005 (0.70)	203	0.00
Ward, days	204	1.67 (1.43)	203	1.55 (1.21)
HDU/ITU, days	203	0.02 (0.28)	203	0.005 (0.07)
Subsequent inpatient stays, *n*	204	0.08 (0.32)	203	0.06 (0.26)
Subsequent day cases, *n*	204	0.24 (0.48)	203	0.28 (0.66)
Outpatient visits, *n*	204	1.29 (1.72)	203	1.18 (1.73)
Outpatient procedures, *n*	204	0.25 (0.61)	203	0.26 (0.56)
Inpatient stays at other NHS hospitals, *n*	151	0.01 (0.11)	144	0.00 (0.00)
Outpatient visits at other NHS hospitals, *n*	151	0.71 (1.48)	144	1.12 (1.70)
Accident and Emergency Department visits, *n*	145	0.08 (0.41)	139	0.09 (0.53)
Face-to-face GP contacts, *n*	136	0.79 (1.85)	128	0.57 (1.66)
Telephone calls with GP, *n*	119	0.33 (1.47)	116	0.16 (0.57)
District nurse visit, *n*	122	0.16 (0.53)	117	0.15 (0.98)
Community-based health service contacts, *n*	117	0.27 (1.26)	110	0.12 (0.60)
Medications, *n*	138	0.05 (0.33)	123	0.03 (0.25)

[a]*The mean resource use is presented rather than absolute numbers or percentages to allow clinicians/decision makers to apply their own costs to the resources used, which improves transparency and aids decision making.* [b]*Simple imputation methods as outlined in Table 1 were used to create the dataset from which the resource use in this table were estimated.*

Table 3 Cost consequence results.[a]

Variable	*N* TURP:ThuVARP	Adj. TURP Mean (95% CI)	Adj. ThuVARP Mean (95% CI)	Adj. difference in Mean (95% CI)
NHS secondary care perspective costs, £	204:203	4244.12 (3985.12, 4503.11)	4252.92 (3992.29, 4513.54)	−8.80 (−376.24, 358.64)
NHS perspective costs, £	204:203	4305.23 (4043.75, 4566.71)	4309.45 (4046.08, 4572.82)	−4.22 (−375.04, 366.60)
QALY	204:203	0.84 (0.82, 0.86)	0.83 (0.81, 0.85)	0.01 (−0.01, 0.04)

[a]*All variables are adjusted (Adj.) for centre and baseline diagnosis. Additionally, QALYs were adjusted for baseline score.*

patients overall spent time in High Dependency Units (HDUs)/Intensive Therapy Units (ITUs), but more time was spent there by patients in the TURP arm. Patients in the TURP arm also had a slightly higher number of subsequent inpatient stays and outpatient visits, and slightly less follow-up daycase admissions than those in the ThuVARP arm, as well as slightly more community-based health service contacts and medications (Table 2).

In the analysis from the secondary care NHS perspective, the total adjusted mean costs in the TURP arm were slightly lower (£4244) than the ThuVARP arm (£4252), a cost difference of just £9 (95% CI –£376, £359) (Table 3). From the wider NHS perspective, which included primary care costs, this cost difference reduces slightly to £4 (95% CI –£375, £366) resulting from the slightly higher community care use in the TURP arm. Men in the TURP arm had slightly more adjusted mean QALYs (0.84) than those in ThuVARP arm (0.83) (Table 3), the difference of 0.01 (95% CI –0.01, 0.04) is equivalent to an extra 4 days of the best imaginable health in favour of TURP during 12 months.

The incremental NMB at a £20 000 per QALY threshold of TURP compared with ThuVARP in relation to the NHS secondary care perspective was £236.24 (95% CI −£419.48, £891.96) and in relation to the wider NHS perspective was £231.57 (95% CI −£429.32, £892.46).

Figures 1 and 2 depict the CEACs for the two different perspectives and indicate that at the willingness to pay threshold of £20 000 per QALY, the probability that TURP was the cost-effective treatment compared with ThuVARP was 76% for the NHS secondary care perspective and 75% for the wider NHS perspective.

The sensitivity analyses (Table 4) showed that with one exception the initial results were robust in that the incremental NMB at a £20 000 per QALY threshold of TURP compared with ThuVARP was positive. In the case of excluding the post-recovery ward costs to examine costing

Fig. 1 NHS secondary care perspective CEAC.

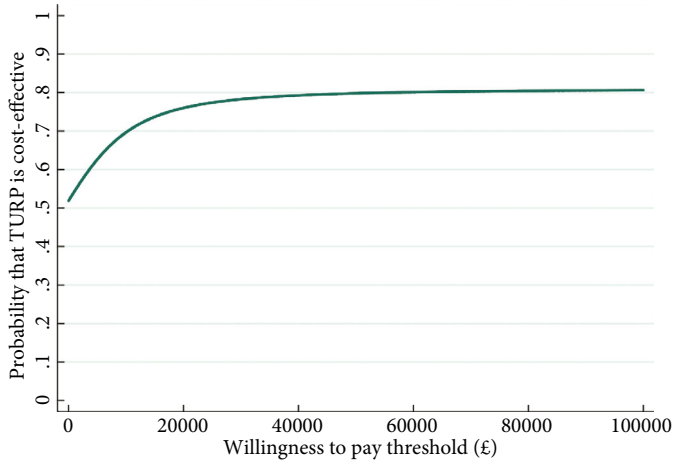
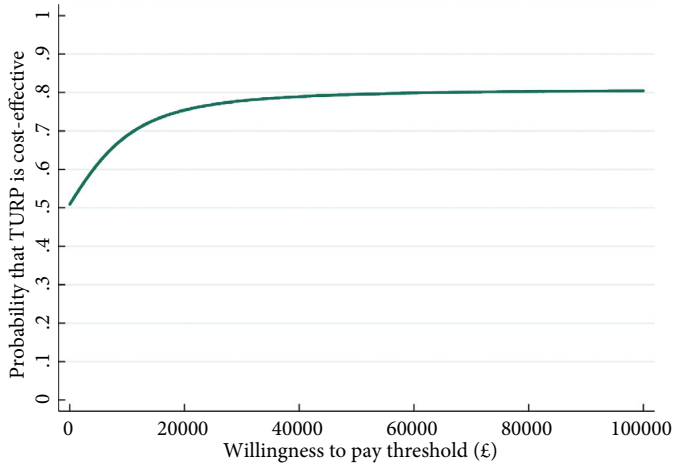


Fig. 2 NHS health care perspective CEAC.



ThuVARP as daycase surgery, TURP was no longer both cheaper and more effective than ThuVARP and had an incremental NMB of −£98.95 (95% CI −£745, £547) at the threshold of £20 000 per QALY. Using an alternative cost for recovery not only increased the cost difference in favour of TURP, but also led to a decrease in overall costs for both arms £2719 (TURP) and £2834 (ThuVARP).

Discussion

The total adjusted mean NHS secondary care costs for the 12 months of the trial within the TURP arm were £9 less than those in the ThuVARP arm, which reduced to £4 when community-based healthcare costs were included. The greater length of time needed to conduct the ThuVARP procedure meant the ThuVARP arm remained slightly more expensive, despite longer recovery time and slightly greater postoperative resource use for patients in the TURP arm. Although these costs were very similar, the slightly lower costs and a slightly higher QALY score within the TURP arm meant the probability that TURP is the cost-effective option is at least 76% at all thresholds at and above £20 000 per QALY. The sensitivity analyses with one exception reinforced the certainty around this result.

The expected lower costs in the ThuVARP arm resulting from an anticipated reduction in hospital stay and potential to be done as a daycase did not materialise. To some extent the ability to conduct ThuVARP as a daycase was affected by an artefact of the trial, as patients in each site had to be listed as daycase or inpatient stays prior to admission because randomisation was conducted at the point of surgery. At two sites both procedures could be listed as a daycase, due to an unrelated move by their respective trusts to conduct TURP procedures as day cases; however, at the remaining five sites all procedures were listed as inpatient stays. In the UK more TURPs are now being conducted as day cases, which could be a reason for an equal mean length of stay (2 days) for TURP and laser procedures within England [26]. Any effect on costs of being able to use a daycase procedure for ThuVARP in five of the centres where daycase TURPs were not being conducted was examined through exclusion of post-recovery ward costs for patients who were randomised to ThuVARP in these five centres. The analysis showed there were lower costs in the ThuVARP arm in this scenario (£3909 vs £4245). This is based on the scenario in these five centres that ThuVARP will always be a daycase procedure. In the two centres in which daycase TURPs were conducted, 47% of ThuVARP procedures were conducted as daycases and there was a mean ward stay of 1.77 days for ThuVARP patients who stayed overnight. There would therefore be a much smaller difference in cost than implied by the sensitivity analysis, as ward costs would be incurred for some ThuVARP patients.

The sensitivity analysis in which the average times of theatre by arm and centre from the last 25% of cases was applied to all other cases confirmed that no learning curve effect was found for ThuVARP. This may have been the result of all surgeons having to complete a training programme before being involved in the trial, which included an independent assessment prior to conducting laser procedures within the trial [27

]. The TURP procedure took on average 21 min less than the ThuVARP procedure; this cumulative effect on an operating list could lead to an extra TURP procedure being put onto each half-day list, helping to reduce time on waiting lists.

During the trial there were 18 laser equipment failures: nine prior to the start of surgery and nine during surgery, which meant a TURP procedure was commenced or these procedures were converted to TURPs. A further 27 conversions to TURP also occurred mainly because of very

Table 4 Sensitivity analysis.

	N	Adjusted mean costs[b], £ Mean (95% CI)	Adjusted QALYs[b] Mean (95% CI)	Incremental Costs, £ (95% CI)	Incremental QALYs (95% CI)	ICER £/QALY	Incremental NMB (£) at £20 000/QALY (95% CI)
Complete case analysis[a]							
TURP	77	3528.74 (3182.88, 3874.61)	0.87 (0.84, 0.90)				
ThuVARP	75	4085.53 (3735.04, 4436.02)	0.84 (0.81, 0.87)	−556.79 (−1051.63, −61.94)	0.03 (−0.009, 0.072)	ThuVARP dominated by TURP	1185.53 (259.87, 2111.18)
The exclusion of prostate cancer-related hospital resource use							
TURP	204	4219.71 (3963.99, 4475.43)	0.84 (0.82, 0.86)				
ThuVARP	203	4192.06 (3934.95, 4449.16)	0.83 (0.81, 0.85)	27.65 (−335.35, 390.65)	0.01 (−0.01, 0.04)	2270.32	215.93 (−451.29, 883.15)
Application of the average times of theatre from the last 25% of cases by arm in each centre, all other cases[c]							
TURP	185	4179.60 (3915.71, 4443.49)	0.84 (0.82, 0.86)				
ThuVARP	183	4252.56 (3986.43, 4518.70)	0.83 (0.81, 0.85)	−72.96 (−447.42, 301.50)	0.01 (−0.02, 0.04)	ThuVARP dominated by TURP	1382.08 (725.31, 2038.85)
Exclusion of post-recovery ward costs for those patients who had a ThuVARP procedure in centres where daycase TURP procedures were not conducted							
TURP	204	4244.57 (3988.76, 4500.39)	0.84 (0.82, 0.86)				
ThuVARP	203	3909.32 (3654.55, 4164.09)	0.83 (0.81, 0.85)	335.25 (−25.54, 696.05)	0.01 (−0.01, 0.04)	£28375.12	−98.95 (−744.81, 546.90)
Excluding the cost of the laser machine and TURP generator							
TURP	204	4238.27 (3979.01, 4497.53)	0.84 (0.82, 0.86)				
ThuVARP	203	4186.80 (3927.69, 4445.91)	0.83 (0.81, 0.85)	51.47 (−315.26, 418.20)	0.01 (−0.01, 0.04)	£4534.61	175.55 (−481.00, 832.10)
Capital and reusable equipment costs based on 100 uses							
TURP	204	4278.79 (4018.28, 4539.30)	0.84 (0.82, 0.86)				
ThuVARP	203	4400.13 (4137.97, 4662.29)	0.83 (0.81, 0.85)	−121.34 (−489.91, 247.22)	0.01 (−0.01, 0.04)	ThuVARP dominated by TURP	343.87 (−298.96, 986.70)
Capital and reusable equipment costs based on 500 uses							
TURP	204	4239.92 (3981.04, 4498.79)	0.84 (0.82, 0.86)				
ThuVARP	203	4209.23 (3949.04, 4469.42)	0.83 (0.81, 0.85)	30.69 (−337.12, 398.49)	0.01 (−0.01, 0.04)	2671.38	199.04 (−451.38, 849.47)
The need for TURP equipment to be available because of failures in ThuVARP equipment							
TURP	204	4243.68 (3983.94, 4503.43)	0.84 (0.82, 0.86)				
ThuVARP	203	4261.36 (4003.38, 4519.33)	0.83 (0.81, 0.85)	−17.68 (−384.08, 348.73)	0.01 (−0.01, 0.04)	ThuVARP dominated by TURP	268.38 (−373.83, 910.59)
The use of an alternative recovery time cost of £2.58/min							
TURP	204	2719.29 (2524.44, 2914.15)	0.84 (0.82, 0.86)				
ThuVARP	203	2833.54 (2637.78, 3029.3)	0.83 (0.81, 0.85)	−114.25 (−390.42, 161.92)	0.01 (−0.01, 0.04)	ThuVARP dominated by TURP	338.67 (−275.89, 953.22)

[a]Including only participants for whom we had complete cost and QALY information. [b]Adjusted for the minimisation variables of the randomisation process: study centre and baseline diagnosis. Additionally, QALYs were adjusted for baseline score. [c]One centre was excluded from this analysis as the last 25% of the operations in one of the arms had missing data for time of operation.

large prostate size (nine patients), bleeding (four), poor visibility (four), and to collect remaining fragments of prostate (four). Although the sensitivity analysis that added the TURP capital costs to those randomised to ThuVARP and received ThuVARP only led to a mean increase in cost of just over £9, the laser appears to be required as an additional rather than a replacement piece of capital equipment.

The present study is the first individual patient economic evaluation within a randomised trial investigating the cost-effectiveness of TURP with ThuVARP for men with BPO. However, the findings in the present study are supported by previous research [28] comparing a non-contact side-firing neodymium:yttrium-aluminum-garnet (YAG) probe to TURP, which found TURP to be the most cost-effective treatment option in terms of symptomatic improvements. Other studies, comparing TURP to other laser procedures have indicated lower costs for the laser procedures: in the United States, photoselective vaporisation of the prostate (PVP) vs TURP ($4266 vs $5097) [29]; in Australia, PVP vs TURP (AU$3368 vs AU$4,292) [30]; and in New Zealand, holmium:YAG laser

resection of the prostate (HoLRP) cost 24.5% less ($651) than TURP [31]. These lower costs have been accredited to the outpatient nature of laser treatment, shorter stays for inpatients, reduced catheterisation time, and lower complication rates. These anticipated benefits of the ThuVARP procedure were not observed in the UNBLOCS trial.

One of the major strengths of the present study was the combination of the use of routine hospital PLICS data for follow-up outpatient visits (including procedures) and inpatient stays, reducing ascertainment bias. This method of data collection also probably led to more complete data for the NHS secondary care analysis and was less burdensome on the research nurses than if a medical notes review had been conducted. Additionally, detailed data collection during surgery by research nurses meant the cost differences between the two operations could accurately be established.

The successful blinding of the patients also meant that their answers to the EQ-5D-5L would not be affected by the knowledge of their treatment allocation.

There may have been an underestimate of uncertainty around theatre costs from the use of simple imputation methods. There were 10 more missing recovery times in the TURP arm, which could have led to a slight overestimate of the TURP costs, although this would not have affected the overall conclusions. Equipment was costed using a list of bipolar TURP equipment, as this was the most common procedure. Even in the hypothetical scenario that monopolar fixed equipment cost per procedure was double that of the bipolar equipment (£15.64) it would not have had a significant effect on the results.

Some uncertainty surrounds the wider NHS analysis. Prior to the creation of the multiple imputed dataset the percentage of cases that had complete NHS resource use was low and differential between arms (43% ThuVARP: TURP 50%). This potentially means that the data may not have been missing at random (MAR), as possibly healthier men were completing the questionnaires, and those in the ThuVARP arm did have a slightly lower quality of life in terms of QALYS. The poor completion of the 3- and 6-month resource use questionnaires, also meant that it was not appropriate to conduct the originally planned analyses from a patient and societal perspective.

The present study has found that, from an NHS secondary care perspective, TURP is the most likely cost-effective option compared with ThuVARP, and there was little uncertainty around this result. This trial provides valuable findings on the short-term cost-effectiveness of TURP compared to ThuVARP and modelling could extrapolate these results over longer time horizons.

The expected reduction in costs of ThuVARP resulting from its ability to be done as a daycase did not materialise and this analysis confirms that TURP remains a cost-effective procedure for men with BPO.

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Conflicts of Interests

Dr Abrams reports grants and personal fees from Astellas, personal fees from Pfizer, personal fees from Ipsen, personal fees from Ferring, personal fees from Pierre Fabre, personal fees from Coloplast, personal fees from Sun Pharma, outside the submitted work. All other authors declare no conflicts of interest.

Data Availability Statement

All data requests should be submitted to the corresponding author for consideration. Access to anonymised data may be granted following review.

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Abbreviations: BPO, benign prostatic obstruction; CEAC, cost-effectiveness acceptability curve; CRFs, Case Report Forms; EQ-5D-5L, EuroQoL five Dimensions five Levels; HDU, High Dependency Unit; HoLEP, holmium laser enucleation of the prostate; HRG, Health Resource Group; ICER, cost-effectiveness ratio; ITU, Intensive Therapy Unit; NICE, National Institute for Health and Care Excellence; NMB, Net Monetary Benefit; PLICS, Patient-linked information costing systems; QALYs, quality adjusted life years; RCT, randomised controlled trial; SUR, seemingly unrelated regressions; ThuVARP, thulium laser transurethral vaporesection of the prostate; TUR, transurethral resection.