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The Continuing Story of the Cost-Effectiveness of Photoselective Vaporization of the Prostate versus Transuretheral Resection of the Prostate for the Treatment of Symptomatic Benign Prostatic Obstruction

J. Andrew Thomas, FRCS[1], *Andrea Tubaro, PhD*[2], *Neil Barber, FRCS*[3], *Andrew Thorpe, FRCS*[4], *Nigel Armstrong, PhD*[5], *Alexander Bachmann, PhD*[6], *Ben Van Hout, PhD*[7,*]

[1]*Department of Urology, Princess of Wales Hospital, Bridgend, Wales, UK;* [2]*Department of Urology, Sant'Andrea Sapienza University, Rome, Italy;* [3]*Department of Urology, Frimley Park Hospital, Frimley, Camberley, Surrey, UK;* [4]*Freeman Hospital Newcastle, Newcastle upon Tyne, UK;* [5]*Kleijnen Systematic Reviews, York, UK;* [6]*Department of Urology, University of Basel, Basel, Switzerland;* [7]*School for Health and Related Research, University of Sheffield, Sheffield, UK*

ABSTRACT

Background: In 2008, a UK assessment of technologies for benign prostatic obstruction concluded negatively about photoselective vaporization of the prostate (PVP), and the 2010 National Institute for Health and Care Excellence guidance caused several UK institutions to abandon PVP. **Objective:** To reassess the costs and effects of PVP versus transurethral resection of the prostate (TURP) on the basis of most recent data. **Methods:** The same model was used as in 2008. Transition probabilities were estimated using a Bayesian approach updating the 2008 estimates with data from two meta-analyses and data from GOLIATH, the latest and largest trial comparing PVP with TURP. Utility estimates were from the 2008 assessment, and estimates of resource utilization and costs were updated. Effectiveness was measured in quality-adjusted life-years gained, and costs are in UK pounds. The balance between costs and effects was addressed by multivariate sensitivity analysis. **Results:** If the 2010 National Institute for Health and Care Excellence analysis would have updated the cost-effectiveness analysis with figures from its own meta-analysis, it would have estimated the change in quality-adjusted life-years at −0.01 (95% confidence interval [CI] −0.05 to 0.01) instead of at −0.11 (95% CI −0.31 to −0.01) as in the 2008 analysis. The GOLIATH estimate of −0.01 (95% CI −0.07 to 0.02) strengthens the conclusion of near equivalence. Estimates of additional costs vary from £491 (£21–£1286) in 2008 to £111 (−£315 to £595) for 2010 and to £109 (−£204 to £504) for GOLIATH. PVP becomes cost saving if more than 32% can be carried out as a day case in the United Kingdom. **Conclusions:** The available evidence indicates that PVP can be a cost-effective alternative for TURP in a potentially broad group of patients.

Keywords: benign prostatic obstruction, cost effectiveness analysis, NICE guidance, health care, United Kingdom.

Introduction

Benign prostatic obstruction (BPO) leading to bothersome lower urinary tract symptoms negatively affects quality of life in older men. Prevalence is more than 50% in men in their sixties, increasing to 90% for those older than 80 years [1,2]. Men aged 40 to 50 years who present with lower urinary tract symptoms have a 20% to 30% chance of ever undergoing a prostatectomy [3].

Typically, medical therapy is the first-line treatment offered. When this fails, standard treatment is transurethral resection of the prostate (TURP). TURP requires anesthesia and 2- to 4-day hospitalization and is associated with several potential complications including transurethral resection syndrome (<1.1%), blood transfusion (2.9%–8.4%), urethral stricture (3.8%), bladder neck contracture (4.7%), retrograde ejaculation (65.4%), impotence (6.5%), urinary incontinence (2.2%), and mortality (0.1%–0.25%) [4].

Consequently, alternative procedures were developed in an attempt to minimize invasiveness, reduce complications, and shorten recovery times. In 2008, the National Institute for Health Research commissioned a health technology assessment (HTA) comparing alternative therapies with TURP. The assessment concluded that "In the absence of strong evidence in favor of newer therapies, TURP remains both clinically effective and cost-effective. The use of minimally invasive technologies in the NHS is not appropriate until a more effective and/or less costly technology is available" [5]. Moreover, it recommended that "A well conducted head-to-head trial of treatment strategies .... would be most desirable to establish the gold standard. Such a

* *Address correspondence to*: Barend Adrianus Van Hout, University of Sheffield, ScHARR, Regent Court, 30 Regent Street, ScHARR' Sheffield S14DA, UK.

E-mail: b.a.vanhout@sheffield.ac.uk., bvanhout@pharmerit.com.

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trial should take prostate size into account and should include direct measures of utility” [5].

Laser vaporization of the prostate was one of the innovative therapies included in the 2008 assessment. The assessment pooled data from multiple laser systems, delivering energy from different light spectrums, resulting in different methods of vaporizing obstructing prostate tissue. A publication summarizing the cost-effectiveness analysis stated, “Potassium titanyl phosphate laser vaporisation was unlikely to be cost effective … which argues against its unrestricted use until further evidence of effectiveness and cost reduction is obtained” [6]. The National Institute for Health and Care Excellence (NICE) guidance that followed in 2010 recommended to “only consider offering laser vaporisation techniques …. as part of a randomised controlled trial that compares these techniques with TURP.” Strangely, although NICE reevaluated the evidence base, eliminating a Dutch study [7] with an atypical rate of incontinence, it did not reevaluate the cost-effectiveness, thereby never noticing the consequences of deleting this Dutch study from the evidence. As a result, utilization of laser vaporization decreased dramatically in the United Kingdom.

Photoselective vaporization (PVP) was one of the systems adding to the evidence base by one study [8]. Since 2008, two significant technological improvements in PVP were introduced: increased laser power and an improved laser delivery system for rapid and hemostatic treatment of large prostate glands. In addition, the largest randomized controlled trial (RCT) comparing PVP with TURP, the GOLIATH trial—a noninferiority study of men with lower urinary tract symptoms due to BPO—was initiated [9]. The clinical manuscript summarizes the results by saying that

> The study demonstrated the non-inferiority of XPS to TURP for IPSS, Qmax (maximum flow rate) and complication-free proportion. PV and PVR were comparable between groups. Time until stable health status, length of catheterisation, and length of hospital stay were superior with XPS ($p < 0.001$). Early re-intervention rate within 30 d was three times higher after TURP ($p = 0.025$); however, the overall postoperative re-intervention rates were not significantly different between treatment arms. Conclusions: XPS was shown to be non-inferior (comparable) to TURP in terms of IPSS, Qmax, and proportion of patients free of complications. XPS results in a lower rate of early reinterventions but has a similar rate after 6 mo. [9]

However, it may be noted that the difference in the International Prostate Symptom Score is borderline, significantly in favor of TURP, and that the secondary end points—concerning symptoms—are also, albeit nonsignificantly, in favor of TURP. So, there may a trade-off between efficacy, safety, convenience, and costs and each aspect may be associated with its own “value.” In 2008, the difficulty to bring together the various risks, disutilities, and costs was acknowledged by the use of a cost-effectiveness model that included all these in a structured and transparent way. The model, a Markov-type model, included parameters concerning baseline risks, probability of success, and incidence of transient and permanent adverse effects as well as estimates of costs and disutilities due to adverse effects. Estimates of efficacy and adverse effects were based on meta-analyses. Now, more RCTs are available, not only GOLIATH using the 180-W system but also four trials using the 120-W system and four that used the 80-W laser system, as included in a 2012 meta-analysis [10].

The emerging situation seems tailormade for a Bayesian approach. Bayesian statistics build on the idea of continuously updating the relevant estimates by combining prior information with new data [11]. The combination of priors with new data leads to posterior distributions in which means or medians can be used as point estimates and 95% credible intervals can be used to indicate the degree of remaining uncertainty. Within this, the posterior distributions of today become the prior distributions of tomorrow. The 2008 data can be used to formulate a “prior” distribution, and to combine this with the “data” from subsequent studies to estimate the current, most up-to-date “posterior” distributions of costs, effects, and the balance between costs and effects. The expectation may be that such stepwise Bayesian approach will iterate to less and less uncertainty. This applies, however, only to a rather stable situation. Medical technologies such as PVP and TURP continuously evolve, and as such prior distributions may reflect only outdated information. One might expect improvements, especially in the active treatment arm but also in the control arm. In addition, one might expect surgeons to broaden the indication, given the increased safety and efficacy. Expert elicitation might be used to capture such phenomena reflected by the inclusion of parameters indicating the improvements in technology and case mix. The analysis presented here does not go that far. The Bayesian case, building on former evidence is the one, rather conservative extreme, building the evidence in time, without acknowledging any progress by weighing newer data more heavily. The other extreme is to use separate chunks of evidence as used in previous analyses and to add the data from the GOLIATH study as another separate chunk. Both approaches will lead to updated estimates of costs and effects, and together they are a source of information for an updated decision of the position of laser therapy for benign prostatic hyperplasia (BPH).

Methods

The Model

The parameters and model used in the 2008 HTA form the basis of this analysis [5]. The model is a state transition Markov-type model with a lifelong time horizon in which patients, after initial treatment, are categorized in mutually exclusive states guided by their urinary symptoms and whether or not they have incontinence symptoms (Fig. 1). In line with the 2008 model, reoperations may be carried out in case of insufficient relief but not in case of persistent urinary incontinence. Also, the use of alpha-blockers and five alpha reductase inhibitors in case of failure is not included except after two treatment failures. Mortality is assumed not to be affected by treatment, and age-specific population mortality rates for English men are used.

The 2008 model was programmed in TreeAge. To gain insight and to optimize computer time, it was reprogrammed in Excel. The only estimates that were not taken from the original model, keeping the structure and most estimates identical, concerned procedural cost parameters, unit cost estimates, and estimates concerning efficacy and safety. The latter estimates were obtained by reading the efficacy and safety data—as reported in Appendix 1—into R and calling WinBugs from R. Multivariate sensitivity analysis was carried out on the basis of 1000 random draws using a macro in Excel.

In case of discrepancies between the publication and the TreeAge program, the TreeAge program was taken as reference. For example, the 2008 TreeAge model used a meta-analysis of all TURP data for the estimate of the incidence of adverse effects, leading to, among others, a baseline rate of urinary incontinence of 151/1935 (=7.8%). This is contrary to the estimate of 0.03 as published in Table 30. Similarly, with respect to the utilities, estimates from the TreeAge code were used (where the 95% confidence intervals are surrounding the point estimates, as one would expect.) Another change is that in the rare case of multiple adverse effects, utilities were estimated by multiplication.

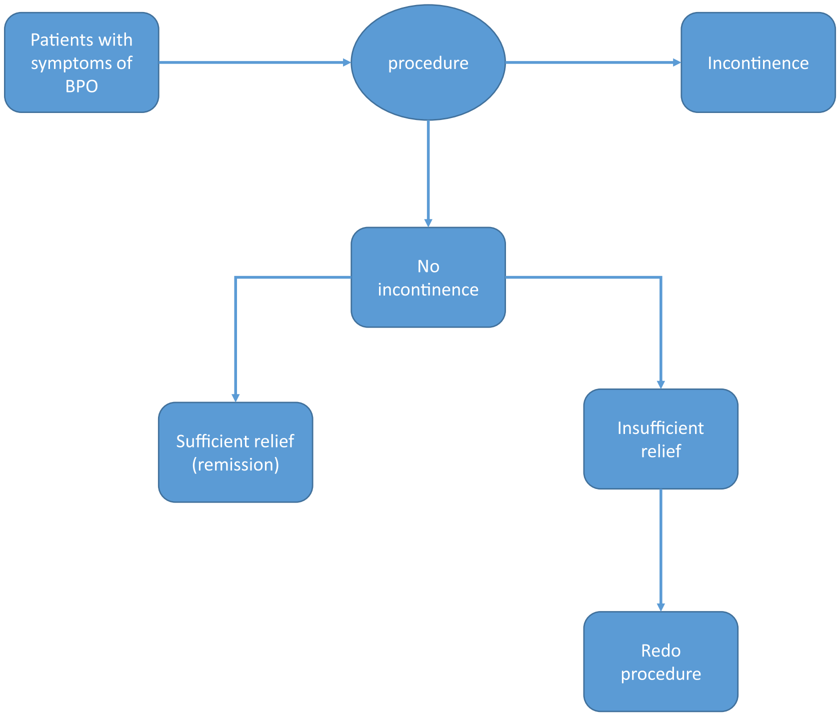

Fig. 1 – Model. BPO, benign prostatic obstruction. (Color version of figure appears online.)

In 2008, the probability of success/failure was arbitrarily estimated on the basis of the number of patients with a 10% or more/less than 10% decrease in the International Prostate Symptom Score. To derive this probability, patient-level data are needed or at least an estimate of the variance of the mean change. In 2008, an estimate of the latter was obtained from a cohort of patients with TURP and in combination with some assumption results that showed face validity were obtained. This was not the case when applying the same method to the later data, potentially due to differences in variance. In 2008, as an alternative, within the sensitivity analysis, success was estimated using the percentage of patients undergoing reoperation. For this, no additional data are needed nor any assumptions. Here, the latter approach is chosen to define the measure of efficacy.

The only permanent complication within the model is the occurrence of persistent urinary incontinence. This was assumed to be known at 3 months after initial treatment and within the model this is the same period when a number of transient complications may occur: the transurethral resection syndrome, acute urinary retention, urinary tract infection, strictures/bladder neck contracture, and blood transfusion. Complications are captured by one-time probabilities associated with the initial procedure. The probability of movement from one state to another is captured by transition probabilities, which reflect the probability of a non–procedure-related-relapse initiating repeat treatment. With subsequent treatments, a decrease in efficacy is taken into account.

A health care perspective is taken. Costs concern those related to the procedure, the length of hospital stay, and the treatment of complications.

Effectiveness is expressed in terms of the percentage of patients without complications and without repeat procedures, the number of incontinent patients at 6 or 12 months, and the expected number of quality-adjusted life-years (QALYs). Both total costs and QALYs are presented with a discount rate of 3.5%.

The time horizon is lifelong. The primary efficacy outcome of the analysis is QALYs. These are estimated by multiplying the duration in each health state with its corresponding utility value. The short-time QALY losses associated with transient adverse effects are included in the valuation of the first 3 months after the procedure.

All analyses compared two strategies: one that starts with TURP and one that starts with PVP, both followed by TURP when indicated.

Data Sources

Data are used from three published meta-analyses and from GOLIATH. All data compare laser vaporization techniques to TURP. The first two sources, analyzing multiple laser vaporization technologies, are meta-analyses included in the 2008 HTA and the 2010 NICE guidance [5,12]. The data underlying a 2012 meta-analysis comprise the third source [13–19]. One-year data from GOLIATH, using 180-W technology, are the fourth source [9].

Importantly, 2008 and 2010 meta-analyses differ in that the latter included a study published in 2008 [13] and most importantly excluded a Dutch study from 2003 [7]. This changed the estimated risk ratio for incontinence from 2.24 (1.03–4.88) to 0.90 (0.26–3.15).

As in 2008, procedure costs are based on reference cost, Personal Social Services Unit (PSSRU), and British National Formulary (BNF) estimates (in 2013 pounds). A weighted average of the number of day cases and inpatient cases was used, with weights obtained from the GOLIATH study. The difference in length of stay and the use of fibers for PVP and loops for TURP was also estimated on the basis of GOLIATH.

Comparisons

Five sets of estimates of baseline and transition probabilities were used to estimate the costs and effects of PVP versus TURP:

1. Those based on the 2008 meta-analysis and used in the 2008 cost-effectiveness model estimates;

2. Those based on the 2010 meta-analysis (but never used in a cost-effectiveness analysis);
3. Posterior estimates of 120-W systems with a prior based on the 2010 and 2012 80-W systems;
4. GOLIATH with uninformed prior distributions; and
5. GOLIATH with the posterior from 3) as prior information.

All data are included in the Appendix.

Within the analysis, attention was drawn to the fact that patients with PVP may be treated in a day-case setting, which is a rare possibility for patients with TURP. The analysis estimates the percentage of day-case procedures required, from which cost savings can be expected.

Statistical Analysis

In 2008, baseline risks were estimated using beta distributions, with risk ratios estimated using a fixed-effects meta-analysis. Here, random-effect models were used for all risk ratios using programs from Warn et al. [20] who describe a Bayesian approach to a random-effects meta-analysis for binary outcomes. Initial risks after TURP were estimated separately. The noninformative approach used a beta distribution for the initial risk, assuming a [0,1] uniform prior and a binomial distribution for the data. This implies that in case of zero events no continuity correction is needed as was the case in 2008. In the informed analysis, the prior is the former posterior. Within the estimation a random component was included (as in a random-effects analysis). The latter was to reflect the additional variation—and uncertainty—that results from the potential difference in surgical skills with respect to TURP.

The distribution of costs and effects was estimated using probabilistic sensitivity analysis drawing at random from the uncertainty distributions that are defined surrounding all input parameters.

Estimates of costs and effects are presented in cost-effectiveness planes and summarized in terms of the probability to be more or less effective, more or less costly, and the probability that the cost-effectiveness ratio is less than (when effects are positive) or more than £20,000 (when effects are negative). The same results are presented for a cost-effectiveness ratio of £30,000.

Results

The estimates concerning baseline risk and risk ratios are presented in Table 1.

The difference between the baseline risks as estimated in 2008 and 2010 is explained by the fact that the 2008 estimates are based on all TURP trials, including those comparing with other treatments, whereas the 2010 estimates are based on TURP trials only in comparison with laser therapy. For example, considering the incidence of incontinence, if only trials comparing PVP versus TURP would have been used, an estimate of 2.46% would have resulted.

The differences between the 2008 and 2010 meta-analyses with respect to risk ratios are mainly explained by differences in the inclusion and exclusion of trails. The 2010 analysis—being 2 years later—included some more recent trials, and it also included one older trial and excluded data from other trials that were included in the 2008 analysis. Details are included in the Appendix in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2015.04.002.

It was expected that the informed analyses would lead to less uncertainty. Surprisingly, it is not seen in baseline risk rates, where the variability in the various trials lead to only small differences in uncertainty between the informed and uninformed GOLIATH analysis. Substantial differences are found in the risk ratios, most notably where laser therapy is shown to decrease the occurrence to almost zero. Attention may be drawn to the risk of the transurethral resection syndrome, which is nonexistent after laser therapy. In the uninformed GOLIATH analysis, it is estimated at 0.64, which is due to the zero event correction. In the informed analysis, it is equal to 0.02. In this respect, the Bayesian approach offers a definite advantage, given that the transurethral resection syndrome can only be the result of a crossover and in the informed analysis this is learned in time. Moreover, instead of a noninformative prior, as used here, an informed prior might have been used, narrowing the uncertainty even further.

Table 2 presents updated UK estimates concerning resource utilization and unit costs as well as some additional parameters. Among the latter are estimates for quality-of-life parameters taken from the 2008 HTA as well as estimates for the probability of requiring TURP after urinary retention, the decrease in efficacy at subsequent procedures, and the probability of a relapse. All estimates are associated with uncertainty distributions, which are used in the multivariate sensitivity analysis.

Figure 2 presents the days of hospitalization in both arms of GOLIATH. The average difference is 1.15 days. This is shorter than the 1.97 days obtained by taking a weighted average of the figures reported in the trials included in the 2012 meta-analysis [10].

Table 3 presents estimates of costs and effects within a lifetime horizon. The 2008 analysis shows a difference of −0.11 QALYs and a 95% upper uncertainty margin of 0.01, which might be labeled as a significantly worse outcome. Similarly, one may label costs as significantly higher, with the lower bound of the 95% credible interval being equal to £21. So, one finds a significantly worse outcome with a significant increase in costs and therefore, the conclusion drawn in 2008 seemed justified. The conclusion in the *BMJ* saying that “The use of … laser vaporisation incurred higher costs and was less effective” and “findings were unchanged by wide ranging sensitivity analyses” was based on this. This is based, however, on a rather unrealistic approximate 18% rate of incontinence after PVP. In contrast, the 2010 and later analyses show that credible intervals for QALY and cost difference cross zero, suggesting with much less certainty that those differences are due to differences in treatment. It may be speculated that this would have led to another conclusion.

Figure 3 shows that all density of costs and effects is in the quadrant of higher costs and less efficacy driven particularly by the 2008 incontinence estimates. It also shows that an updated cost analysis using the 2010 meta-analysis would have shifted estimates to the right. One may still not conclude that this implies equivalence, but such a picture may—when considering additional arguments such as convenience—lead to a different conclusion.

Figure 4 indicates the changing levels of uncertainty surrounding costs and effects as new evidence becomes available, starting from the 2010 meta-analysis. It appears that GOLIATH has not shifted the results toward more efficacy or lower costs. It also appears that the decreased uncertainty of the informed analysis has not resulted in a spectacular change in overall uncertainty when compared with the uninformed analysis.

Table 4 presents percentages in the four quadrants of the cost-effectiveness plane. With the 2008 estimates, the probability of cost-effectiveness being in an acceptable range (cost-effectiveness ratio <£20,000 or both more expensive and less costly) is very low, 0.065%, and the decision that it is not cost-effective is straightforward. For 2010, it is estimated at 28% and when using results from the 120-W technology; informed by the 80-W technology, an estimate of 52% results. This decreases again to about 30% when using the informed GOLIATH analysis. Using a higher threshold of £30,000 does not alter the results substantially.

Table 1 – Baseline risks and risk ratios.

Baseline risks	2008 meta-analysis		2009 meta-analysis		120 W informed by 80 W		GOLIATH		GOLIATH informed	
	Point estimate (%)	95% credible interval (%)	Point estimate (%)	95% credible interval (%)	Point estimate (%)	95% credible interval (%)	Point estimate (%)	95% credible interval (%)	Point estimate (%)	95% credible interval (%)
Reoperation	4.56	3.56–5.23	4.72	1.73–10.43	2.65	1.00–5.76	3.30	1.14–7.56	3.01	1.40–5.68
Incontinence	7.80	6.17–8.39	1.12	0.22–3.50	1.06	0.24–3.08	2.99	1.00–6.99	2.60	1.07–5.35
AUR	4.42	3.34–5.23	1.58	0.48–3.90	4.63	1.42–11.39	9.69	5.63–15.60	8.53	5.08–13.44
BNC	6.25	4.95–6.88	6.26	3.48–10.40	7.46	2.71–16.58	6.80	3.43–12.16	7.23	4.09–11.88
Blood transfusion	8.10	6.54–8.51	3.59	0.95–9.58	4.68	1.57–10.94	1.59	0.28–5.16	2.39	0.94–5.06
TUR syndrome	2.04	1.27–2.88	6.26	3.48–10.40	2.65	0.56–7.92	0.37	0.00–2.52	1.01	0.27–2.67
UTI	7.17	5.54–7.94	7.45	2.59–17.03	7.03	2.72–15.05	10.65	6.27–16.97	10.60	6.69–15.99
Risk ratios	**2008 meta-analysis**		**2009 meta-analysis**		**120 W informed by 80 W**		**GOLIATH**		**GOLIATH informed**	
	Point estimate	**95% credible interval**	**Point estimate**	**95% credible interval**	**Point estimate**	**95% credible interval**	**Point estimate**	**95% credible interval**	**Point estimate**	**95% credible interval**
Reoperation	1.59	0.97–2.62	1.55	0.57–3.43	1.62	0.56–3.72	1.74	0.43–4.82	1.66	0.64–3.58
Incontinence	2.24	1.03–4.88	1.38	0.11–6.19	0.70	0.09–2.65	1.55	0.34–4.58	1.31	0.38–3.33
AUR	2.89	1.55–5.42	7.21	2.03–18.60	2.27	0.59–6.14	1.21	0.57–2.28	1.41	0.71–2.51
BNC	0.54	0.32–0.90	0.28	0.05–0.91	0.61	0.16–1.64	0.95	0.33–2.17	0.80	0.34–1.62
Blood transfusion	0.14	0.05–0.42	0.05	0.00–0.32	0.04	0.00–0.18	0.19	0.00–1.14	0.04	0.00–0.16
TUR syndrome	0.33	0.01–7.93	0.28	0.05–0.91	0.03	0.00–0.19	0.64	0.00–2.65	0.02	0.00–0.11
UTI	1.17	0.60–2.26	1.00	0.22–2.96	1.03	0.32–2.52	1.75	0.91–3.06	1.66	0.93–2.74

AUR, acute urinary retention; BNC, bladder neck contracture; TUR, transurethral resection; UTI, urinary tract infection.

Table 2 – Estimates of unit costs and utilities.

Unit of resource utilization	Point estimate	95% credible interval	Distribution	Source
Procedure costs				
Procedure with overnight stay	£2,317	£2307–£2326	Lognormal	Elective inpatient, LB25C, TURP without CC, reference costs
Procedure as day case	£1,097	£1025–£1175	Lognormal	Day case, LB25C, TURP without CC, reference costs
% of TURPs as day case	2.97%	2.74%–3.19%	Beta	TURP without CC, reference costs
Loop				
Monopolar	£50	£40–£60		Hospital information
Bipolar	£180			Hospital information
Fiber	£550			Hospital information
Average length of stay with TURP	4.09	3.64–4.54	Normal	GOLIATH
Average length of stay with PVP	2.94	2.52–3.37	Normal	GOLIATH
Costs of complications (£)				
Incontinence, monthly	108	82–134	Triangular	Update of NICE Guideline 2010
Bladder pressure test	147	112–182	Lognormal	Outpatient procedures, LB42A, reference costs
Blood transfusion	736	561–911	Triangular	Update of NICE Guideline 2010
1-d hospital stay	296	226–367	Lognormal	Excess bed day, elective inpatient, LB25C, reference costs
Outpatient attendance	94	72–116	Lognormal	Consultant led follow-up, 101, urology, reference costs
Artificial sphincter	5005	3816–6193	Lognormal	Elective inpatient, LB21Z, reference costs
1-d high dependency unit	631	481–781	Lognormal	Critical care services - XC07Z, adult critical care, reference costs
No remission, monthly	26	20–33	Triangular	Update of NICE Guideline 2010
Loop (electrode)	60	46–74	Uniform	Hospital information
Decrease in efficacy second procedure (%)	25	0.00–50.00	Triangular	Lourenco et al. [5]
10-y relapse rate (%)	8	7.50–8.50	Triangular	Lourenco et al. [5]
Length of stay				
Transurethral resection syndrome	2.5	2–3	Uniform	Expert opinion
Laser therapy	2.6	2–3	Negative binomial	UK data from GOLIATH
TURP	4	3–5	Negative binomial	UK data from GOLIATH
Utilities				
No remission	0.94	0.92–0.96	Beta	Lourenco et al. [5]
Incontinence	0.89	0.88–0.91	Beta	Lourenco et al. [5]
Bladder neck contracture	0.95	0.95–0.96	Beta	Lourenco et al. [5]
Acute urinary retention	0.89	0.87–0.92	Beta	Lourenco et al. [5]
Transurethral resection syndrome	0.81	0.77–0.85	Beta	Lourenco et al. [5]
Urinary tract infection	0.93	0.92–0.94	Beta	Lourenco et al. [5]

CC, complication; NICE, National Institute for Health and Care Excellence; PVP, photoselective vaporization of the prostate; TURP, transurethral resection of the prostate.

Slightly more favorable results are obtained when further scrutinizing underlying data. Horasanli et al. [13] report seven reoperations after PVP and zero after TURP. Al-Ansari et al. [16] report six redo PVP after PVP and one redo after TURP. Within the experience of the clinical authors, both results may be interpreted as reflecting an imbalance in surgeon experience between PVP and TURP and thus noninformative for capturing routine practice. As a type of sensitivity analysis, one may calculate the results when omitting these trials from the analysis. This decreases the risk ratio for repeat operations from 1.66 (0.64–3.58) to 1.38 (0.51–3.04). In that case, the probability of being more effective increases from 25.05% to 30.10% and the probability of an acceptable cost-effectiveness ratio with a £20,000 threshold increases from 25.45% to 30.00%.

From the most recent data included in "Informed GOLIATH," the additional costs are estimated at £130 and the probability of cost saving is estimated at 20%. This is estimated with 16% of patients with PVP as a day case and 2.97% for TURP. When the percentage of PVP day cases is increased to 32%, as strongly supported by "time to stable health status $<$ 24 hours" [9], of more than 70% of the patients with PVP in the United Kingdom, PVP and TURP show equal costs.

Discussion

At the turn of the 21st century, PVP therapy using an 80-W GreenLight laser system appeared to be a promising new technique for the treatment of symptomatic BPO, resulting in reduced catheterization times, hospitalization, and the possibility of day-case surgery. It also offered high-risk patients a viable surgical alternative to the standard-of-care TURP.

The 2008 HTA concluded that PVP was unlikely to be cost-effective and the subsequent 2010 NICE directive, with no new

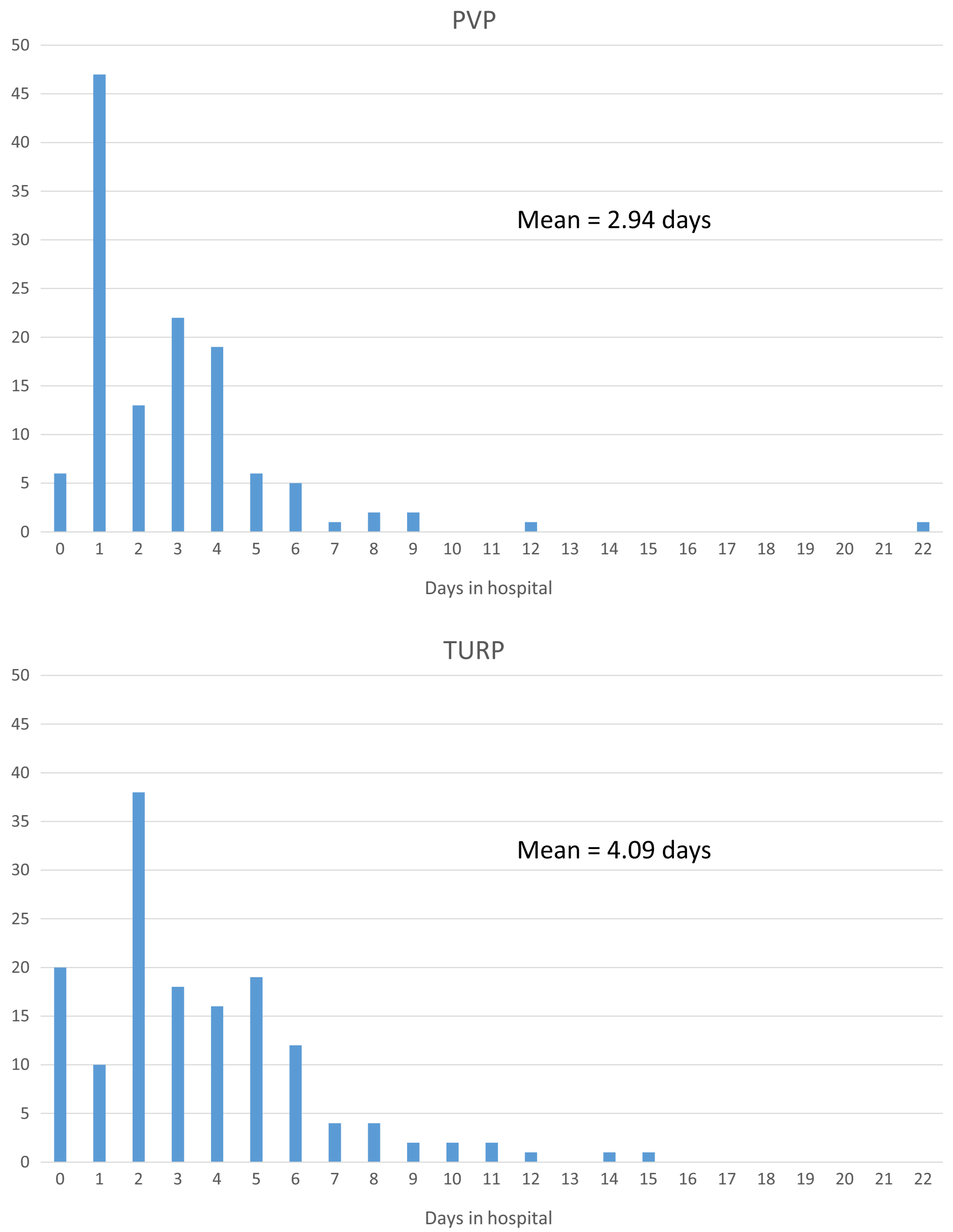

Fig. 2 – Days in hospital (GOLIATH). PVP, photoselective vaporization of the prostate. (Color version of figure appears online.)

cost-effectiveness analysis despite an updated meta-analysis, suggested limiting PVP in the National Health Service to controlled research settings only. It may be noted that this was mainly based on the combination of a baseline estimate of incontinence after laser therapy of 17.51%, which resulted after multiplying the estimated baseline rate of 7.8% with an estimated relative risk of 2.34. This figure—which was used in the calculations—is in contrast with the average estimate of incontinence in the trials, which was 5.88%. Moreover, the baseline risk as well as the risk ratio was affected by the inclusion of a Dutch trial that registered rates of incontinence of 14/45 after PVP and 4/50 after TURP. Although these figures suggest a significant difference, the text surrounding them does not and the abstract of this trial states: "No clinically relevant differences were found between these modalities." This is probably also the reason why the incontinence data from this trial were excluded from the 2010 meta-analysis and this explains the decrease in the risk ratio from a rather significant 2.24 to a rather uncertain 1.38.

A restriction of use may, nevertheless, have been the right advice in 2008— considering that there was only one RCT for PVP in its most recent form (Bouchier et al. [8]). Interpretations and calculations, however, suggested too much certainty. Our calculations show that if the 2010 meta-analysis would have been used for a reevaluation of costs and effects, there would have been a lot less superfluous certainty. It would still point into a negative direction, but one might wonder whether the conclusions would have been milder and would have kept PVP usage at a higher rate than it has been within the United Kingdom over the last few years.

In spite of the UK position, GreenLight laser development continued and the 120-W high performance system (HPS) version was developed in other countries. The GOLIATH RCT comparing

Table 3 – Baseline results.

	2008 meta-analysis			2010 meta-analysis (80 W)			120-W informed			GOLIATH (180 W)			GOLIATH (180 W) informed		
Outcome	TURP	Laser	Diff	TURP	Laser	Diff	TURP	Laser	Diff	TURP	Laser	Diff	TURP	Laser	Diff
Years without symptoms	8.51	7.53	−0.99	9.17	9.03	−0.13	9.29	9.26	−0.03	9.06	8.82	−0.24	9.10	8.97	−0.12
Years without incontinence	8.74	7.81	−0.93	9.43	9.38	−0.04	9.45	9.48	0.03	9.25	9.09	−0.16	9.29	9.21	−0.08
Complications (%)															
AUR	4.56	13.20	0.09	1.63	11.83	0.10	4.77	10.88	0.06	10.00	12.15	0.02	8.80	12.41	0.04
BNC	6.45	3.48	−0.03	6.47	1.82	−0.05	7.69	4.67	−0.03	7.01	6.69	0.00	7.46	5.98	−0.01
Blood transfusion	8.36	1.16	−0.07	3.71	0.19	−0.04	4.83	0.21	−0.05	1.64	0.32	−0.01	2.47	0.10	−0.02
TUR syndrome	2.10	0.70	−0.01	6.47	1.82	−0.05	2.73	0.09	−0.03	0.38	0.25	0.00	1.04	0.02	−0.01
UTI	7.39	8.62	0.01	7.71	7.75	0.00	7.25	7.47	0.00	10.99	19.26	0.08	10.94	18.22	0.07
QALYs	9.72	9.60	−0.11	9.79	9.78	−0.01	9.80	9.80	0.00	9.78	9.75	−0.03	9.78	9.77	−0.01
Lower 95% limit	9.71	9.41	−0.31	9.76	9.72	−0.05	9.78	9.76	−0.03	9.75	9.69	−0.13	9.73	9.62	−0.07
Upper 95% limit	9.75	9.72	−0.01	9.81	9.81	0.01	9.82	9.82	0.02	9.80	9.80	0.03	9.81	9.80	0.02
Costs of initial procedures (£)	2,283	2,347	63	2,283	2,347	63	2,283	2,347	63	2,283	2,347	63	2,403	2,455	51
Costs due to complications (£)	319	300	−20	287	249	−38	331	287	−44	342	358	17	359	350	−9
Repeat procedures (£)	290	291	1	313	348	35	285	309	24	288	315	27	306	322	16
Incontinence (£)	334	712	377	55	71	16	45	33	−12	128	193	65	111	144	32
Lack of remission (£)	111	180	69	95	129	34	60	79	19	76	111	35	76	95	19
Costs (£)	3,338	3,829	491	3,033	3,144	111	3,004	3,054	50	3,117	3,324	207	3,256	3,365	109
Lower 95% limit	3,196	3,269	21	2,910	2,818	−315	3,074	3,003	−373	2,858	2,656	−223	2,801	2,622	−204
Upper 95% limit	3,337	4,556	1,286	3,346	3,912	£595	3,427	3,805	£489	3,253	3,722	702	3,263	3,524	504

AUR, acute urinary retention; BNC, bladder neck contracture; Diff, difference; QALYs, quality-adjusted life-years; TUR, transurethral resection; TURP, transurethral resection of the prostate; UTI, urinary tract infection.

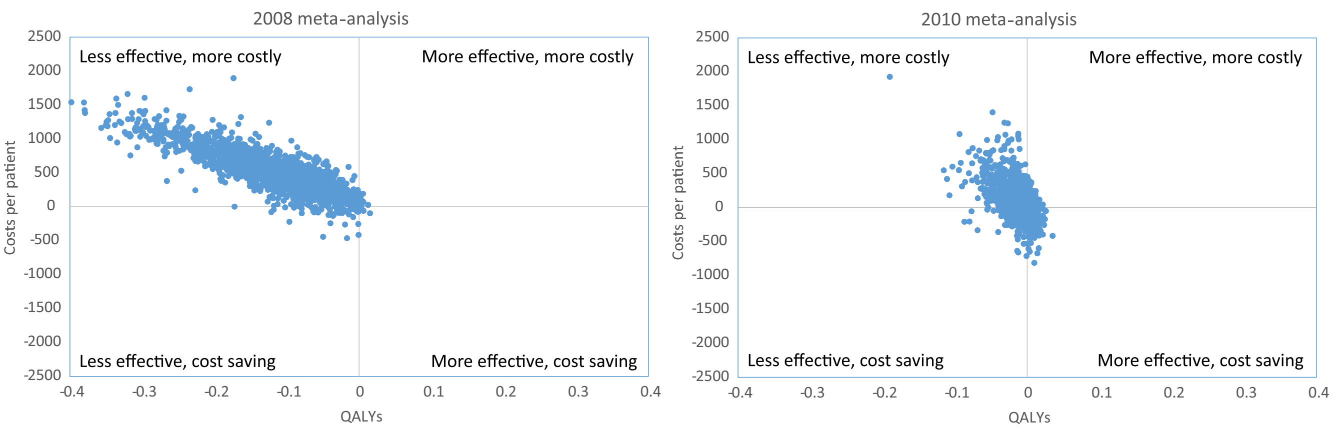

Fig. 3 – Costs and effects based on 2008 and 2010 meta-analyses. QALYs, quality-adjusted life-years. (Color version of figure appears online.)

the 180-W PVP to TURP for relatively low risk/standardized patient selection with symptomatic BPO concludes noninferiority compared with TURP at 6-month follow-up.

When confronted with the problem, a negative study in 2008, continuous developments in time, and at the end, the GOLIATH study, a Bayesian approach sounded attractive. This study shows that this may not be as straightforward. Both treatments under consideration have developed. PVP now has a more efficient fiber delivery system and 100% more power. Similarly, TURP can now be performed using bipolar technology in saline irrigation. Even with this knowledge, no clear trends are found. This may be due to not only patient selection but also surgeon experience (e.g., Horasanli et al. [13]): The low rate of adverse events for TURP in GOLIATH (transfusion rates 0.75% vs. expected 2.9% [9]) was achieved through careful patient selection and surgery by experienced consultant surgeons only. In contrast, individual surgical experience with PVP varied from 10 to 500 cases. Despite this, PVP was shown to be noninferior to TURP. Such considerations might need to be captured in the priors considering the various parameters and further study may be needed to do so.

With respect to patient selection, it may also be noted that the GOLIATH study and earlier studies have been carried out in patients in whom TURP is an option. This excludes patients with

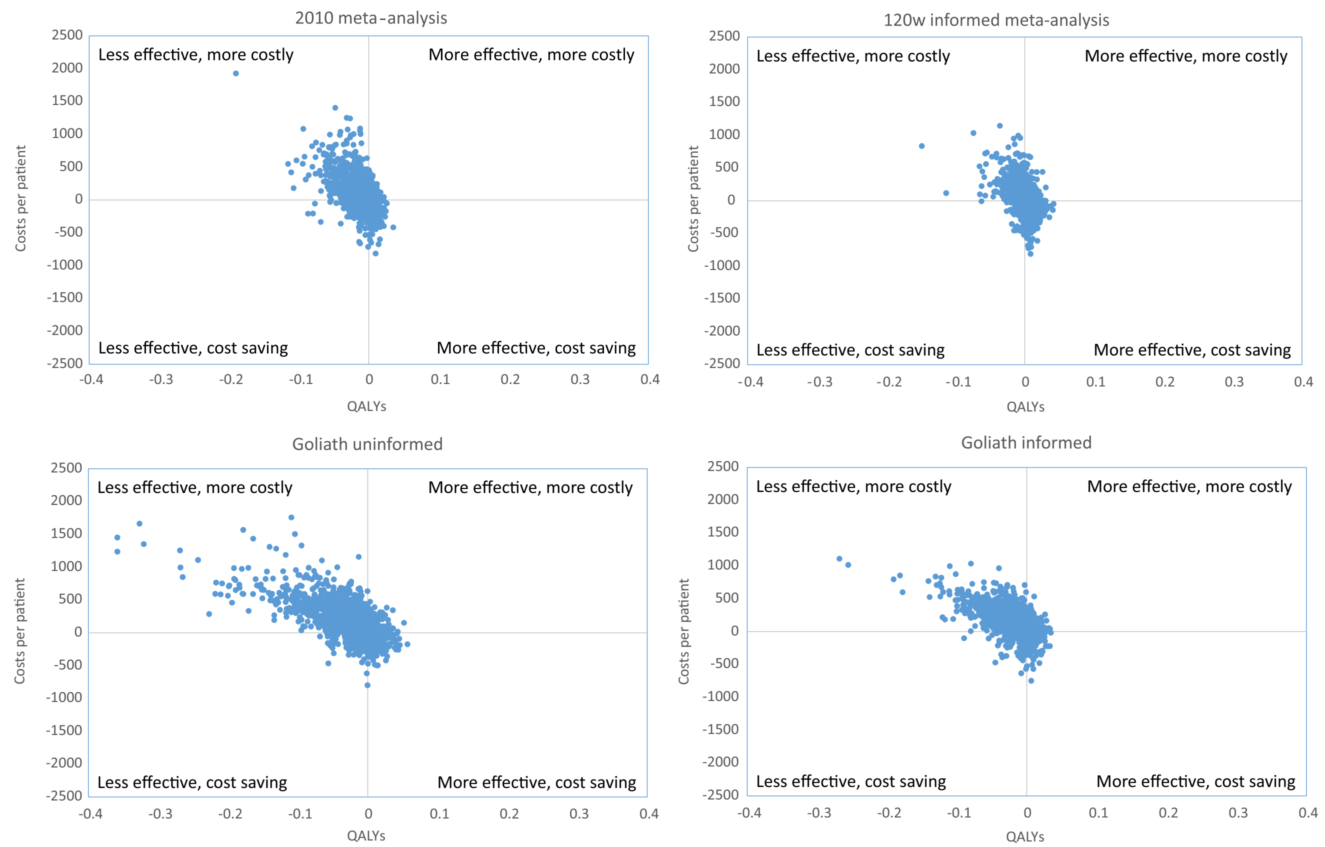

Fig. 4 – Costs and effects with different sources of information about effectiveness. QALYs, quality-adjusted life-years. (Color version of figure appears online.)

Table 4 – CE results.

Effectiveness	Costs		2008 meta-analysis (80 W)	2010 meta-analysis (80 W)	120-W informed by 80 W	GOLIATH (180 W)	GOLIATH (180 W) informed
Less effective	More expensive		96.95	55.25	31.70	64.25	60.90
	Less expensive		1.75	20.00	12.00	10.55	9.00
		CE ratio > £20,000	0.15	8.50	6.35	2.70	9.00
		CE ratio > £30,000	0.15	6.90	4.95	2.15	9.00
More effective	More expensive						
		CE ratio < £20,000	0.40	4.20	11.30	7.35	9.75
		CE ratio < £30,000	0.60	5.10	13.10	9.00	11.90
	Less expensive		0.50	15.75	35.05	11.60	11.00
Acceptable	At a threshold of £20,000		1.05	28.45	52.70	21.65	29.75
	At a threshold of £30,000		1.25	27.75	53.10	22.75	31.90

Note. All values are in %.
CE, cost-effectiveness.

multiple comorbidities, a group for whom PVP is a real alternative. This may need a different analysis but will likely be cost-effective (given the acceptance of TURP as an intervention in these patients).

The QALY analysis within this comparison has copied the approach as followed in 2008. The results still show a favorable albeit nonsignificant outcome for TURP. Here other aspects, such as the significant difference in "time to stable health status < 24 hours," may enter the equation. Moreover, although day-case treatment has not been within the remit of GOLIATH, 70% of the UK patients had "time to stable health status < 24 hours." This potential convenience for both patients and hospital may also need consideration. It is estimated that when more than 32% of the cases can be treated as a day case, savings can be expected. In addition, one might consider the benefits this has in the loss of working days or time to return to daily activities. Finally, one may want to consider that the analysis as presented here does not include the heterogeneity of the patient population as well as differences in treatment setting. The analysis suggests a one-size-fits-all-situations approach and this is unlikely to apply. Especially with TURP, some patients are predictably at a higher risk of some adverse events and consequently clinicians may—by careful selection—optimize the balance between costs and effects. The biggest benefits may be in patients for whom TURP is too risky, patients who did not enter the trials. The GOLIATH study, as well as earlier studies, has been carried out in patients in whom TURP is an option. This excludes patients with multiple comorbidities, a group for whom PVP is a real alternative. Starting from the results of the analysis presented here, it is envisaged that if one accepts TURP as an intervention in those patients, PVP will likely be cost-effective. Naturally, this will need further substance and the model as presented here might be used to further define what information exactly would be needed [21–29].

Conclusions

Caution is needed in the use and interpretation of meta-analyses that consider the efficacy of procedures that evolve in time such as PVP and—to a lesser extent—TURP. The current evidence suggests that over the last 10 years PVP has almost caught up with TURP. The differences in symptom score are now small, albeit still in favor of TURP. Differences in convenience are evidently in favor of PVP. Moreover, although the costs—as assessed in the GOLIATH trial—are almost equal, PVP can easily be carried out as a day case and when organized as such, it is expected to lead to considerable savings. The current restrictions on the use of PVP need to be reevaluated in light of these data.

Supplemental Materials

Supplemental material accompanying this article can be found in the online version as a hyperlink at http://dx.doi.org/10.1016/j.jval.2015.04.002 or, if a hard copy of article, at www.valueinhealthjournal.com/issues (select volume, issue, and article).

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