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Medical technology consultation: GID-MT564 GreenLight XPS for treating benign prostatic hyperplasia

Supporting documentation – Committee papers

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

1. **Original EAC assessment report** – an independent report produced by an external assessment centre who have reviewed and critiqued the available evidence.
2. **EAC assessment report update –**an independent report update produced by an external assessment centre who have reviewed and critiqued the available evidence.
3. **Assessment report overview** – an overview produced by the NICE technical lead which highlights the key issues and uncertainties in the company's submission and assessment report.
4. **Scope of evaluation** – the framework for assessing the technology, taking into account how it works, its comparator(s), the relevant patient population(s), and its effect on clinical and system outcomes. The scope is based on the sponsor's case for adoption.
5. **Company submission of evidence** – the evidence submitted to NICE by the notifying company.
6. **Expert questionnaires** – expert commentary gathered by the NICE team on the technology.
7. **EAC correspondence log** – a log of all correspondence between the external assessment centre (EAC) and the company and/or experts during the course of the development of the assessment report.
8. **Company fact check comments** – the manufacturer's response following a factual accuracy check of the assessment report.

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

External Assessment Centre report

Title: GreenLight XPS 180-W for prostate vaporisation in benign prostatic hyperplasia

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Declared interests of the authors

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Rider on responsibility for report

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

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1 Summary

Scope of the sponsor's submission

The clinical context is the treatment of benign prostatic obstruction (BPO) from benign prostatic enlargement (BPE), caused by the histological condition of benign prostatic hyperplasia (BHP). For the main indication in average risk patients the sponsor considered appropriate patients, the intervention was GreenLight 180-W treatment compared to transurethral resection of the prostate (TURP) and appropriate outcomes were reported. For the secondary indication in high risk patients, the sponsor only considered patients on anticoagulants or antiplatelets rather than all patients with a bleeding risk, and did not consider patients with larger prostates.

Summary of clinical evidence submitted by the sponsor

Four studies were submitted by the sponsor, one RCT of GreenLight 180-W vaporisation (vs TURP) for average risk patients and 3 case series (1 study evaluating GreenLight 180-W and 2 studies evaluating 120-W) for high-risk subgroups of patients.

Summary critique of clinical evidence submitted by the sponsor

The RCT was of higher quality and gave useful information but the case series were of lower quality and 1 was irrelevant as it included insufficient high-risk participants. One of the case series had useful comparative information on patients taking anticoagulants and/or antiplatelets vs those who were not.

Searches by the EAC revealed an additional RCT in average risk patients on GreenLight 180-W treatment compared to TURP and 10 case series for high risk groups of patients, of which 4 yielded useful comparative information. Two of the case series were using GreenLight 120-W treatment in patients taking anticoagulants and/or antiplatelets and two were using GreenLight 180-W treatment in patients with larger prostates. The EAC also found an RCT of GreenLight 180-W vapo-enucleation vs HoLEP, an off-label use of GreenLight treatment but the only evidence on GreenLight 180-W treatment available for the comparator appropriate to high risk subgroups. The second RCT was using GreenLight 120-W treatment in larger prostates.

There is sufficient information to suggest that GreenLight 180-W treatment is clinically similar in effectiveness and adverse events to TURP and that it takes longer operating theatre time than TURP but is associated with shorter post-operative catherisation and hospital stay. In high risk subgroups there is insufficient information to know whether there is equivalent hospital stays,

treatment effectiveness or similar rates of adverse events with GreenLight 180-W treatment in patients taking anticoagulation treatment, with larger vs smaller prostates compared to HoLEP or in patients presenting with urinary retention compared to those without.

Summary of economic evidence submitted by the sponsor

Two economic studies were submitted. The first study (Thomas et al 2015) used data primarily from the GOLIATH trial. This study was a state-transition Markov-type model populated using four different sets of data including from the GOLIATH RCT, and was an update to an HTA published in 2008 by Lourenco et al. A Spanish economic study (Benejam-Gual et al. 2014a) which was a multi-centre retrospective cost analysis was also included in the Sponsor's submission.

Summary critique of economic evidence submitted by the sponsor

The first included study (Thomas et al 2015) had patients with BPO when medical therapy had failed. The patients included in the study came from 9 European countries (UK, Germany, France, Italy, Netherlands, Spain, Belgium, Austria, Switzerland) and it evaluated GreenLight XPS 180-W treatment compared to TURP. The resource use included procedure costs (hospital setting), costs of complications (treated at hospital and/or primary care) and quality of life (utilities). A state-transition Markov-type model with a lifelong time horizon was used. Various sources of data were used in an attempt to provide robust estimates of cost-effectiveness. The EAC found several issues with the correctness of the input parameters used. Moreover, omission of capital costs from the analysis makes the findings relevant to those contexts/situations only where no capital costs are actually incurred in adopting the technology. Sensitivity analyses showed a mixed picture. The authors of the Thomas et al (2015) study, themselves, advised caution in using the findings from their study. One of the most relevant GOLIATH trial results used in the study found that the costs were almost equal, but if GreenLight 180-W treatment led to more than 32% of patients being discharged as a day case in the UK context, it became cost-saving. Therefore, the main driver of the cost-effectiveness appears to be the proportion of cases that could be carried out as day cases.

The second included study (Benejam-Gual et al. 2014a) was a Spanish multi-centre retrospective cost-analysis with a 3-month time horizon. How resources were collected and valued and what underlying assumptions were made to arrive at the total costs were not reported in enough details in order

for the EAC to draw any robust conclusion. The results obtained seem to have been influenced by two of the four hospitals in which the length of hospital stay was one day or less for all patients treated with GreenLight XPS 180-W. The average length of stay of 1.31 days is substantially shorter than that observed in the GOLIATH trial (Bachmann et al 2014). Finally, the exclusion criteria coupled with forced statistical methods (trimmed averages) yielded very small standard errors around the costs. This appears to be far from real practice where one would expect some patients to have longer lengths of stay (they are not “extreme values” that could just be “removed”). Despite serious limitations, the study is indicative that GreenLight XPS 180-W may potentially have shorter lengths of stay than TURP and may thus be cost-saving.

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

The clinical evidence submitted by the sponsor for average risk patients was relatively robust in that it came from a RCT in appropriate patients and compared GreenLight 180-W treatment to TURP (the GOLIATH RCT). The clinical evidence submitted for high risk patients was much less robust in that it came from comparative case series and there was no useful information on the relative effectiveness of GreenLight 180-W treatment compared to HoLEP.

The economic evidence submitted by the Sponsor came from the GOLIATH trial, National Reference costs, Hospital Episode statistics and some published literature. Where data were unavailable, the Sponsor consulted with the experts and also provided their internal (academic in confidence) data. Overall, in the average risk group model, the submitted evidence is robust. This is not the case in high risk group model.

The Sponsor also submitted economic evidence in the form of a *de novo* cost model. The model was populated largely with data from the GOLIATH trial but also included relevant parameters from the National Reference costs, Hospital Episode statistics and some published literature. Where data were unavailable, the Sponsor consulted with the experts and also provided their internal (academic in confidence) data. Overall, in the average risk group model, the submitted evidence appears to be robust.

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

The EAC conducted extensive additional searches which resulted in finding additional relevant evidence for average and high risk subgroups of patients. These were analysed and characteristics of the studies and relevant comparative results reported for patients taking anticoagulants and/or antiplatelets, for patients with larger prostates and for patients with or without urinary retention at presentation. The EAC critically appraised the RCT of GreenLight 180-W enucleation vs HoLEP (Elshal 2015), a RCT of GreenLight 120-W vaporisation compared to HoLEP in patients with larger prostates (Elmansy 2012) and a recent systematic review of HoLEP vs TURP (Li 2014). The EAC also conducted a comparative review of 180-W vs 120-W GreenLight treatment, evaluating 5 relevant studies.

While evaluating the economic component, the EAC reviewed additional studies, verified the sponsor's search strategy and inclusion criteria and did independent searches. The EAC validated the sponsor's economic model and reconstructed the decision tree for clarity as well as a validity check. In a de novo cost analysis the GOLIATH trial data reported in Bachmann (2014) were reanalysed and used in the re-constructed model. A threshold analysis was also performed to establish the proportion of day case discharge following surgery after which GreenLight 180-W treatment became cost-saving.

2 Background

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

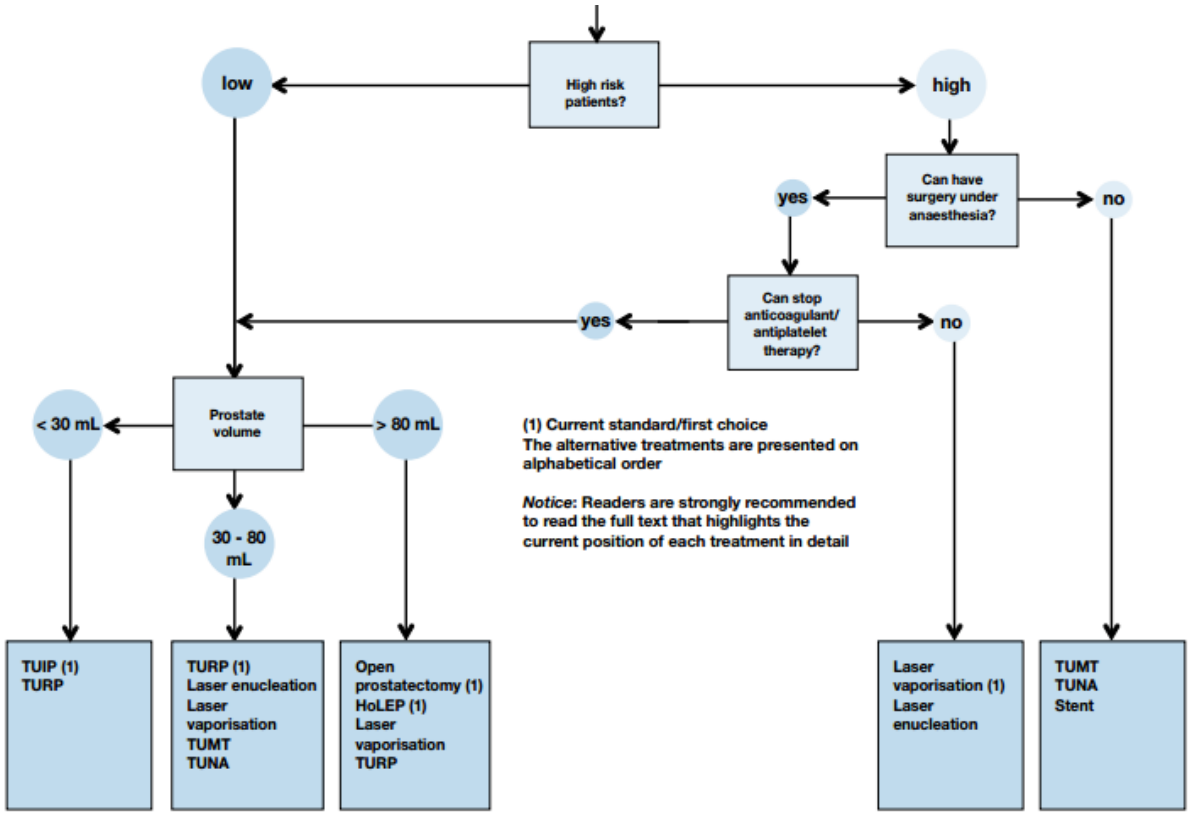
The clinical context is the treatment of benign prostatic obstruction (BPO) from benign prostatic enlargement (BPE), caused by the histological condition of benign prostatic hyperplasia (BHP). There are several ways BPE can be treated. NHS Choices lists behaviour change (including avoiding drinking before sleeping, stopping alcohol and caffeinated drinks, regular exercise and bladder training), medication (finasteride, dutasteride, alpha blockers) and surgery (transurethral resection of the prostate (TURP), transurethral incision of the prostate (TUIP), open prostatectomy, Holmium laser enucleation of the prostate (HoLEP) and laser vaporisation (usually GreenLight laser vaporisation)) (NHS Choices 2015). Surgery is indicated if the patient has moderate to severe symptoms of BPE that have failed to respond to medication (NHS Choices 2015). In the UK, approximately 41% of men aged over 50 will have LUTs and the prevalence rises with age, with 38% aged 61-70 having LUTs rising to 51% over the age of 80. The prevalence of BPH in the UK also rises with age, with 11% of men aged 61-70 rising to 25% aged over 80 years (Trueman 1999). Having BPE is not a risk factor for prostate cancer (Schenk 2011).

The sponsor's description of the clinical context includes a description of BHP, lower urinary tract symptoms (LUTS) and bladder outflow obstruction (BOO). There are some relevant epidemiological statistics given on these conditions. There is a description of the relevant guidelines, particularly from NICE and the European Association of Urology (EAU). The sponsor correctly states that the NICE guidelines recommend that laser vaporisation should only be used as part of a randomised controlled trial (RCT) that compares it to TURP (NICE 2015). The sponsor also correctly shows that the EAU guideline on the surgical management of non-neurogenic male LUTS including BPO has different recommendations. These recommendations can be described in the form of a treatment algorithm and are shown in Figure 1 (reproduced from the sponsor's submission which has been copied from the EAU guidelines). It can be seen that laser vaporisation is the current or first choice therapy in some circumstances and a possible alternative treatment in others. The American Urological Association guideline also states that photoselective vaporization (PVP), for example with the GreenLight laser, is an appropriate and effective treatment alternative to TURP (AUA 2010).

The sponsor correctly states that there is inconsistency between these surgical treatment guidelines. They suggest that an appropriate care pathway would be that PVP with GreenLight would be an appropriate treatment to be offered in all patients with BPE indicated for surgical interventions. High risk

patients should be offered GreenLight PVP or HoLEP as the preferred modalities. The sponsor's description of the clinical context is appropriate and relevant to the decision problem under consideration.

Figure 1. EAU guideline surgical treatment algorithm



Laser vaporisation includes GreenLight, thulium, and diode lasers vaporisation;
Laser enucleation includes holmium and thulium laser enucleation.

TUMT – transurethral microwave therapy, TUNA – transurethral needle ablation. TUIP - transurethral incision of the prostate

2.2 Overview of sponsor's description of ongoing studies

A search of clinical.trials.gov on 8/10/2015 yielded the following ongoing studies:

- GreenLight 180-W vs HoLEP, RCT NCT02332538. The trial is currently recruiting participants (aims for 150 participants) and is due to finish by January 2017.
- GreenLight 180-W vs plasma kinetic vaporization of the prostate using bipolar system, RCT NCT02283684. The trial is currently recruiting

participants (aims for 110 participants) and is due to finish by November 2016.

- GreenLight 180-W vs saline bipolar vaporization (BiVAP) of the prostate, phase 4 RCT NCT01500057. The trial is currently recruiting participants (aims for 60 participants) and is due to finish by February 2016.

- GreenLight 180-W vs HoLEP, non-randomised study in patients with a bleeding tendency (patients allocation based on size of prostate), NCT02293759. The study is currently recruiting participants (aims for 60 participants) and is due to finish by January 2016.

The submission only discusses ongoing studies in the context of the Goliath RCT (Thomas et al, 2015) where all relevant papers have been published. They do not give their search strategy and do not mention any ongoing studies in participants with BPE and concurrent anticoagulant use.

2.3 Critique of sponsor's definition of the decision problem

Population and subgroups

The patient population in the NICE final scope is: People with urinary outflow obstruction secondary to BPH in whom surgical intervention is indicated especially those with larger prostates. The subgroups to be considered are:

- People at risk of bleeding sequelae (including people on anti-coagulation therapy, with a history of bleeding disorders, those with a history of atrial fibrillation, an implanted prosthetic heart valve, implanted coronary stents, patients on aspirin therapy for prior coronary events, patients with prior deep vein thrombosis (DVT) or a high risk of DVT, stroke survivors, haemophiliacs, and patients practising the Jehovah's Witness religion)

- People with a prostate size greater than 100 ml

- People in urinary retention at presentation

The Sponsor's submission selection criteria for published studies were:

a) Men with lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) (primary search)

b) Men with lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) currently on anticoagulants, with prostate glands > 100ml, or in urinary retention (secondary search)

Intervention

The intervention in the NICE final scope is the GreenLight XPS laser system.

The Sponsor's submission selection criteria for published studies were GreenLight XPS 180-W System (patient indication a)) and GreenLight XPS 180-W System or GreenLight HPS 120-W System (patient indication b)).

The GreenLight XPS Laser System is designed for the ablation and coagulation of soft tissue using light, for example in BPO. The Laser System consists of a console, which generates the green laser light and a fibre optic delivery device that transmits laser light from the console to the patient. The console is a Solid State Laser using a neodymium-doped yttrium aluminium garnet (Nd:YAG) laser, which generates a 532 nanometre (nm) output beam. The pulse duration is ~100 nanoseconds and the pulse energy is ~8milliJoules at maximum power (180 Watts (W)). The laser can also be described as a lithium triborate laser. The console generates visible green 532nm laser light. In vaporization mode the power settings range from 20-W to a maximum power determined by the fibre delivery device. In coagulation mode the power settings range from 5 to 40W. Laser energy emission and system status changes are activated through a surgeon controlled, colour-coded footswitch or a system touch screen feature. The first GreenLight lasers had a power of 80W, which were then superseded by the 120-W and now the 180-W devices. The 120-W laser system uses a standard 28mm fibre delivery device whereas the 180-W laser system uses a 42mm MoXy fibre with an internal cooling mechanism with no external water connection, to ensure safe operating temperatures and a longer fibre life. The MoXy fibre system provides a wider tissue vaporization effect without sacrificing the depth of vaporization and coagulation compared to the fibres used with the 120-W system, resulting in the removal of twice as much tissue over the same lasing time.

The GreenLight technology has CE Mark for the indication specified in the scope issued by NICE. This CE Mark was received April 29, 2010.

The sponsor has satisfied the regulatory requirements in the submission and all relevant documents have been submitted (CE Mark Certificate and Certificate of Registration of the Quality Management System (ISO-13485:2003)).

Comparator(s)

The comparators in the NICE final scope are monopolar or bipolar transurethral resection of the prostate (TURP) and holmium laser enucleation of the prostate (HoLEP).

The Sponsor's submission selection criteria for published studies did not include mention of the comparators. The submission does not discuss the lack of comparators and there is no clinical opinion or survey presented.

Outcomes

The outcome measures in the NICE final scope include:

- length of hospital stay
- rate of re-admission
- rate of dysuria (pain)
- duration of catheterisation
- procedural blood loss and blood transfusion requirement
- rate of TUR syndrome
- symptoms of BPH (International Prostate Symptom Score [IPSS] and International Prostate Symptom Score Quality of Life [IPSS-QOL], change in prostate volume, maximum flow rate (Qmax), post-void residual volume (PVR))
- rate of capsular perforation
- frequency of completion as a day case
- quality of life
- device related adverse events

There are no outcome measures listed in the Sponsor's submission selection criteria.

Cost analysis

The sponsor submission includes a cost model, applied to average risk population and high risk population (as a sub-group analysis) separately. The average risk population model compares GreenLight XPS 180-W with TURP (bipolar or monopolar) and high risk model compares GreenLight XPS 180-W with HoLEP.

The sponsor's approach to cost analysis largely reflects the scope. The comparator, perspectives and settings are included within *de novo* model appropriately. The costs are estimated on a per patient basis, assuming that differences in outcomes will be similar in both alternative technologies after six months. The model time horizon - although appears to be reasonable for the purpose of this evaluation - is thus limited to six months.

The submission provides deterministic sensitivity analyses under different scenarios of day case to inpatient ratios. The sensitivity analysis carried out by the sponsor is around some arbitrary credible intervals defined for clinical and cost parameters.

Special considerations, including issues related to equality

The outcome measures in the NICE final scope include that the GreenLight XPS laser system is indicated primarily for use in men over the age of 50, because this is the group in whom histological BPH is most prevalent. This is a function of the clinical condition for which the technology is indicated, and is not likely to be considered an equalities issue. LUTS secondary to BPH is more prevalent in black men than men of white or Asian origin. This is also a function of the clinical condition, not of the technology itself.

Laser vaporisation technology such as GreenLight has the potential to reduce the risk of bleeding compared with other surgical options and so allows transurethral surgery to be undertaken on previously excluded groups, such as those on anticoagulant therapies, those with bleeding disorders and those whose beliefs prevent them from receiving blood transfusions, many of whom may be covered under the 2010 Equality Act.

No equalities issues were raised by the sponsor.

There was no evidence submitted on participants' ethnicity and this is a relevant issue as the condition is more prevalent in black men. There was no evidence submitted demonstrating that GreenLight is equally effective in all ethnic groups, or on any potential differential rates of adverse events in different ethnic groups.

3 Clinical evidence

3.1 Critique of the sponsor's search strategy

The search strategy submitted by the sponsor consisted of electronic database searches only. The databases searched were Medline (Pubmed, Medline In-Process and another version of Medline), Embase and The Cochrane Library (presumably Central). The searches were limited to English language only. There was insufficient information to replicate the searches.

The search terms used for the 'primary' search (for scope population without subgroups) was P – unspecified, I – GreenLight XPS 180-W, C – unspecified, O – unspecified, S – RCTs only (clinical filters were used to limit to RCTs). The search dates were from 2010 to 26th August 2015.

The search terms used for the 'secondary' search (for scope population subgroups) was P – on anticoagulants, I – GreenLight XPS 180-W, C – unspecified, O – unspecified, S – clinical trials. The search dates were from

an unspecified date to 26th August 2015. Search term synonyms used were supplied and are appropriate.

There were no specific searches for adverse events. No unpublished sources of evidence were used. The primary search strategy was appropriate. Additional searches yielded no new includable searches. The secondary search strategy was not appropriate as several additional studies were found (see section 3.9).

3.2 Critique of the sponsor's study selection

The techniques used to select studies are not given, such as the number of reviewers doing the inclusion decisions. There are PRISMA flow diagrams for the included and excluded studies for the primary and secondary searches. However, in the primary searches the numbers seem contradictory in that there were fewer records identified after removing duplicates (n=13) than the number of records screened (n=32). There was a record identified through other sources but the source is unclear. The secondary searches seemed to have found remarkably few records from the databases (n=3).

Inclusion criteria

The evidence submitted for the primary search (Bachmann 2014, Bachmann 2015, Thomas 2015) has the patient inclusion criteria of men with lower urinary tract symptoms due to BPO with prostate volumes less than 100ml and no history of intermittent urinary catheterisation.

The comparator evidence submitted for primary search (Bachmann 2014, Bachman 2015, Thomas 2015) has the comparator of TURP.

The outcomes evidence submitted for primary search (Bachmann 2014, Bachmann 2015, Thomas 2015) had primary outcomes of IPSS, Qmax and being complication-free at 180 days. They also reported PVR, PSA change, adverse events, operating parameters, urinary incontinence, erectile function, quality of life (QoL), costs and patient recovery results.

The evidence submitted for the secondary search (Chung 2012, Woo 2011, Woo 2008) has the patient inclusion criteria of men with BPO and taking antiplatelet/anticoagulant medication (Chung 2012) or coumadin (Woo 201) or men with large prostates (>80ml) and taking anticoagulants (Woo 2008). Patients were recruited in Australia (Chung 2012, Woo 2011) or in 6 countries (Australia, Germany, Spain, Switzerland, UK, USA)(Woo 2008).

There was no evidence submitted on men with BPO with a prostate size greater than 100 ml, and on men at risk of bleeding sequelae who are not on drug treatment, i.e. with a history of bleeding disorders, or atrial fibrillation, an

implanted prosthetic heart valve or coronary stents, with prior deep vein thrombosis (DVT) or a high risk of DVT, stroke survivors, haemophiliacs or patients practising the Jehovah's Witness religion. There was no evidence submitted on participants' ethnicity in any of the included studies.

The evidence submitted for the secondary search (Chung 2012, Woo 2011, Woo 2008) was in the form of case series which had no intervention comparators.

The outcomes evidence submitted for secondary search had outcomes of IPSS, QoL, Qmax, PVR, hospital discharge and adverse events (Chung 2012), IPSS, QoL, Qmax, PVR and adverse events (Woo 2011) and IPSS, Qmax, PVR, prostate volume and complications (Woo 2008).

The inclusion criteria are appropriate for the primary search but are not appropriate for the secondary search in that they yielded a subset of includeable studies.

Additional searches yielded 1 RCT on GreenLight 180-W treatment in BHP (Jovanovic 2014), 7 studies on patients with BPO at high risk, using the 120-W GreenLight laser (Bouabdallah 2013, Cakiroglu 2013, Chen 2013a, Chen 2013b, Sohn 2011, Tam 2012 and Tao 2013). Bouabdallah 2013 is in French but the remaining 6 are in English. Additional searches also yielded 3 case series on patients with BPO with larger prostates, using the GreenLight 180-W laser (Altay 2015, Nicholson 2015, West 2015). Details of these studies are in Section 3.9.

3.3 Included and excluded studies

For the primary searches there was 1 included study (GOLIATH trial) which was a large multicentre RCT. It was reported in 3 publications giving trial results at 6 month (Bachmann 2014), 1 year (Bachmann 2015) and 2 years (Thomas 2015).

For the secondary searches there were 3 included case series (Chung 2012, Woo 2011, Woo 2008), using the 180-W (Chung 2012) or 120-W GreenLight laser (Woo 2011, Woo 2008). No excluded studies were mentioned in the primary searches and one publication was excluded in the secondary searches but the reference was not given. Table 1 gives details of the three included studies.

Table 1. Details of the 3 included case series on high risk patients

Study	Patient population	Country	Age	Study design	Sample size
Chung 2012	Patients on anti-platelet or anti-coagulant therapy, from a larger database of patients who received GreenLight 180-W laser therapy in 2011.	6 centres in Australia	Median age 70, (IQR 65-75)	Retrospective case series with total sample results given at surgery and 3 month follow up.	Total sample 85, 37 on anti-coagulants or anti-platelets
Woo 2011	Patients on warfarin, from a larger database of patients who received GreenLight 120-W laser therapy between 2006-2010.	1 centre in Australia	Mean age 73.4 yrs (range 55-90)	Retrospective case series with total sample results given at surgery and 3 month follow up.	43 taking warfarin
Woo 2008	Subgroups of case series of patients with LUTS associated with BPH using EAU or AUA criteria, with large prostates (>80 ml) and/or on anti-coagulants. All received GreenLight 120-W laser treatment	8 centres in 6 countries (England, Australia Germany, Spain, Switzerland, USA)	Total sample mean age not given. Subgroup results suggest mean age ~70 yrs.	Comparative cohort study with prospective follow up over 11 months.	Total sample size 305, 70 on anti-coagulants, 52 with a larger prostate volume

3.4 Overview of methodologies of all included studies

Primary indication

The GOLIATH trial was a multicentre RCT of men aged 40-80 years, with LUTS due to BPE who had a prostate volume less than100 ml and were not on active anticoagulation therapy. Participants had to have an IPSS score greater than or equal to 12 measured at the baseline visit, medical record documentation of Qmax < 15 ml/s and PV ≤ 100 ml by transrectal ultrasound (TRUS), classified American Society of Anaesthesiologists I, II or III, and a serum creatinine that was within the normal range for the study centre.

Patients were recruited in 9 countries in Europe including the UK (the others were Austria, Belgium, France, Germany, Italy, The Netherlands, Spain, Switzerland).

Exclusion criteria for the study were life expectancy of less than 2 years, currently enrolled in, or planned to enroll in, any concurrent drug or device study, active infection (e.g. urinary tract infection or prostatitis), diagnosis of, or had received treatment for, chronic prostatitis or chronic pelvic pain syndrome (e.g. non-bacterial chronic prostatitis), had been diagnosed with a urethral stricture or bladder neck contracture within the 180 days, or two or more urethral strictures and/or bladder neck contractures within 5 years, diagnosis of lichen sclerosis, neurogenic bladder or other neurological disorder impacting bladder function, polyneuropathy (e.g. diabetic), history of lower urinary tract surgery, diagnosis of stress urinary incontinence that required treatment or daily pad/device use, had a history of intermittent self-catheterization, had been catheterized or had post void residual urine > 400 ml in the 14 days prior to the surgical procedure, had a current diagnosis of bladder stones, had a diagnosis of prostate cancer or a history of carcinoma in situ, TaGII or any T1 stage bladder cancer, had damage to external urinary sphincter, had a medical contraindication for undergoing either TURP or XPS surgery, had a disorder of the coagulation cascade (e.g. haemophilia) or disorders that affect platelet count or function (e.g. Von Willebrand's disease) that would put the subject at risk for intraoperative or postoperative bleeding, unable to discontinue anticoagulant and antiplatelet therapy preoperatively (3–5 days) except for low dose aspirin (e.g. ≤ 100 mg), had had an acute myocardial infarction, open heart surgery or cardiac arrest less than 180 days prior to the date of informed consent, or was immunocompromised (e.g. organ transplant, leukaemia).

The intervention was photoselective vaporization of the prostate (PVP) conducted by GreenLight 180-W laser and MoXy fibres. The comparator was either monopolar or bipolar TURP. The primary outcomes were IPSS, Qmax and being complication-free at 180 days. They also reported PVR, PSA change, adverse events, operating parameters, urinary incontinence, erectile function, quality of life (QoL), costs and patient recovery parameters. These are appropriate outcomes to report.

Results were summarised in the form of numbers and percentages or means and standard deviations. For some parameters such as IPSS, QMax and complication-free proportion, non-inferiority was used to justify one-tailed tests. These result in a p value that is more likely to be less than 0.05. The fact that one-tailed test were used for the main outcome measures was only mentioned in the initial publication (Bachmann 2014). By the 2-year results

publication (Thomas 2015) the secondary analyses were done using the more conventional two-tailed analyses but the primary analysis was still one-tailed.

High risk subgroups

The study by Chung et al (2012) was a retrospective case series from 6 centres in Australia. It included all men undergoing surgical treatment for LUTS due to BPH, with some taking oral anticoagulants or anti-platelets. Men with a history of prostate cancer were excluded. All participants had received GreenLight 180-W therapy between July and August 2011. There was no intervention comparator. Outcomes reported at 3 months included IPSS, QoL, Qmax, PVR and complications classified by Clavien-Dindo grade (Dindo 2004). Statistical analysis was performed using Microsoft Excel 2011. Where comparisons were made, the Student's t-test was employed, but with one-tailed tests, with statistical significance defined at the level of $P < 0.05$.

The study by Woo et al (2011) was a retrospective case series from 1 centre in Australia. Patients on warfarin were selected from a larger database of an unknown number of patients who received GreenLight 120-W laser therapy between 2006 and 2010. No other details of inclusion and exclusion criteria were given. There was no comparator. Outcomes reported at 3 months included IPSS, QoL, Qmax, PVR and adverse events. Results were given as means with standard deviations. Statistical analysis was performed using the Statistics Online Computational Resource (http://socr.ucla.edu/ SOCR.htmal). Mann-Whitney nonparametric tests were used to analyse IPSS, QoL, Qmax, and PVR difference between baseline and outcomes at 3 months. A two-sided P value <0.05 was considered statistically significant.

The study by Woo et al (2008) was a comparative case series from 8 centres in 6 countries (England, Australia Germany, Spain, Switzerland, USA). Patients with LUTS associated with BPH using EAU or AUA criteria were enrolled and subgroups of patients with large prostates (>80 ml) and/or on anti-coagulants were compared to those without these high risk factors. Excluded were patients suspected of having prostate cancer because of raised PSA levels and/or with suspicious lumps found by digital rectal examination. Also excluded were patients with known neurological disorders such as Parkinson's disease or multiple sclerosis, and patients with a history of spinal cord injury. All patients received GreenLight 120-W laser treatment. There was no intervention comparator. Patients were followed up for up to 11 months. Outcomes reported included IPSS, Qmax, PVR, prostate volume and adverse events. Results were given as mean (SD) or number of cases (percentage). Statistical analyses were performed using SPSS 15.0 software package (SPSS Inc., Chicago, IL, USA). Analysis of variance was used for testing numerical data. Related variables were compared using the Wilcoxon

signed-rank test. For categorical data, chi-square tests were used. A two-sided p value < 0.05 was considered to be statistically significant.

3.5 Overview and critique of the sponsor's critical appraisal

Primary indication

The critical appraisal of the GOLIATH trial by the sponsor looked at randomisation, allocation concealment, blinding, similarity of baseline characteristics, differential drop outs, non-reporting of outcomes and intention-to-treat (ITT) analysis. The critical appraisal conducted by the sponsor was appropriate and adequately summarised the blinding issues and how ITT was conducted.

Allocation of patients to treatment arms was by sealed envelope rather than computerised off-site allocation. The implications of a 1-tailed statistical analysis were not discussed.

High risk subgroups

The critical appraisal of the studies in this section used the CASP checklist for cohort studies, which is an appropriate checklist to use. The CASP cohort checklist has 12 questions but they only used 7 of them and split one of them into two questions. The questions they missed were: Does the study addressed a clearly focussed issue?; What are the results of the study?; Do you believe the results?; and the three questions on external validity – Can the results be applied to the local population?; Do the results of this study fit with other available evidence?; and What are the implications of this study for clinical practice?

For the questions they did answer, the discussions of recruitment, exposure and outcomes was appropriate for all three studies. They did not discuss potential confounding factors and mentioned duration of follow up in response to this question for Woo 2008 and Chung 2012 but duration of follow up is not a confounding factor. For Woo 2011, they also mention co-morbidities but do not discuss these and the implications on the results of the study. For all three studies they say that follow up of participants was complete, but also that some were lost to follow up, which is contradictory. For precision of results they report that p values were given but not how wide the estimates of effectiveness were.

The critical appraisal misses some important points. For example, only Woo 2008 gives the background characteristic of age, whereas Chung 2012 and Woo 2011 give no information on the background characteristics at all. Therefore no information on potential confounding factors was available. In Woo 2008 a comparison was made between patients on anticoagulants vs

not, but apart from age, we do not know if the anticoagulant group were comparable to the non-anticoagulant group. It is likely that the anticoagulant group might have had more cardiovascular co-morbidities which would have affected their recovery from operation. In Chung 2012 the case series is on 85 men but only 37 took anticoagulants or anti-platelets. The results are given for all 85 men, most of who were followed up for the outcomes reported. A comparison was not made between men on anticoagulants/anti-platelets compared to those who were not. Therefore the results are not useful for estimating the effect of GreenLight laser treatment in a high risk group.

3.6 Results

The GOLIATH trial surgical operation mean (SD) procedure time results for GreenLight 180-W patients was 49.6 (21.8) minutes compared to 39.3 (18.5) minutes for TURP patients, a statistically significant difference ($p<0.001$). The length of catheterisation for GreenLight 180-W patients was 40.8 (71.5) hours compared to 59.5 (40.6) hours for TURP patients, a statistically significant difference ($p<0.001$). The mean (SD) length of hospital stay for GreenLight 180-W patients was 65.5 (63.3) hours compared to 96.9 (62.0) hours for TURP patients, a statistically significant difference ($p<0.001$). This indicates that although using GreenLight takes longer in the operating theatre, the post-operative recovery time is shorter.

The numerical results from the GOLIATH trial follow ups at 6, 12 and 24 months can be seen in

Table 2 (taken from Thomas et al 2015). The outcome measures are standard ones commonly used in research on BPH and are explained in Appendix 1. Appendix 1 also has a list of minimally important difference magnitudes for the common outcome measures.

The GOLIATH RCT results show that there are slightly higher IPSS, lower Qmax, higher PVR, higher prostate volume, worse quality of life, worse urinary incontinence and worse erectile dysfunction results in GreenLight 180-W patients compared to TURP patients but few of these results are statistically significant. It is unclear whether the result differences are clinically important or not, based on the minimally important difference magnitudes for the common outcome measures in Appendix 1. Fewer patients with GreenLight 180-W treatment had complications compared to TURP patients but more had surgical retreatments for obstruction over the 2-year follow up. Non-inferiority was maintained for the primary outcome measures of IPSS, Qmax and proportion of patients classified complication free (at 6 and 12 months) (Thomas et al 2015).

Results for the GOLIATH study were not given for high-risk subgroups of men taking anticoagulants or antiplatelets, men with larger prostates or men in urinary retention. Men unable to discontinue anticoagulants or antiplatelets and men with post void residual urine > 400 ml in the 14 days prior to the surgical procedure were specifically excluded from the trial.

The comparator for the Goliath study was bipolar or monopolar TURP and comparisons with the intervention are not reported separately for mono0polar and bipolar TURP: this would in any case have been inappropriate the statistical design powered for such an analysis. The TURis MTG23 (NICE 2015) has recognised that the evidence demonstrated the clinical equivalence of bipolar (TURis) and monopolar TURP for prostatic resection.

Table 2. Results of the GOLIATH trial (Thomas et al 2015)

Outcome measure	Arm	6 month	1 year	2 year
IPSS (mean (SD))	GreenLight 180-W	6.8 (5.2) (n=136)	6.9 (6.0)	6.9 (6.0)
	TURP	5.6 (4.9) (n=133)	5.7 (5.3)	5.9 (6.1)
Qmax (mean (SD))	GreenLight 180-W	23.3 (10.1) (n=136)	22.9 (10.7)	21.6 (10.7)
	TURP	24.3 (11.4) (n=133)	24.7 (10.1)	22.9 (9.3)
PVR (mean (SD))	GreenLight 180-W	38.4 (50.0) (n=132)	42.8 (56.9) (n=129)	45.6 (65.5) (n=128)
	TURP	34.6 (50.6) (n=129)	33.4 (43.7) (n=125)	34.9 (47.1) (n=119)
Prostate volume (mean (SD))	GreenLight 180-W	23.0 (11.7) (n=132)	21.9 (11.0) (n=100)	23.9 (13.0) (n=123)
	TURP	20.5 (11.7) (n=127)	21.0 (12.7) (n=102)	22.4 (13.3) (n=117)
PSA (mean (SD))	GreenLight 180-W	1.4 (1.5)# (n=130)	1.3 (1.3) (n=129)	1.4 (1.7) (n=126)
	TURP	1.0 (0.9)# (n=127)	1.1 (1.0) (n=126)	1.1 (0.9) (n=119)
IPSS-QoL (mean (SD))	GreenLight 180-W	1.5 (1.4) (n=134)	1.4 (1.4) (n=129)	1.3 (1.2) (n=127)
	TURP	1.2 (1.2) (n=130)	1.2 (1.3) (n=126)	1.2 (1.3) (n=120)
ICIQ-UI SF (mean (SD))	GreenLight 180-W	3.0 (4.1)# (n=132)	3.3 (4.5)# (n=128)	2.8 (4.1) (n=122)
	TURP	1.7 (2.8)# (n=128)	2.1 (3.3)# (n=122)	2.0 (3.3) (n=118)
IIEF-5 (mean (SD))	GreenLight 180-W	Nr	12.9 (7.5) (n=129)	12.9 (7.5) (n=124)
	TURP	Nr	14.2 (8.2) (n=121)	13.9 (8.2) (n=119)

Complication-free (percentage)	GreenLight 180-W	87.3% (117/134)	84.7% (111*/131)	83.6% (107*/128)
	TURP	83.2% (109/131)	80.5% (102*/127)	78.9% (95*/121)
Surgical retreatments for obstruction (numbers)	GreenLight 180-W	4 (n=131)~	6 (n=124)~	4 (n=58)~
	TURP	7 (n=125)~	2 (n=120)~	1 (n=60)~
* calculated from percentages. # p<0.05 2 sided between group test, ~ number of patients at risk from Kaplan Meier graph so calculation of percentages would be misleading. Nr – not reported				

High risk subgroups – patients on anticoagulants and/or antiplatelets

As Chung 2012 had only 44% of patients taking anticoagulants and/or antiplatelets, and results were not presented separately by anticoagulant/antiplatelet use versus none, there are no relevant results to be reported here.

For Woo 2011 the mean (SD) duration of hospital stay was 32 (38.0) hours. The baseline and 3 month results for 27 of the 43 men in the study are shown in Table 3. For Woo 2008 the mean (SD) duration of hospital stay was not given. The results at average follow up of 4.2 months and percentage change from baseline are also shown in Table 3.

There is insufficient information to determine whether patients taking anticoagulants or antiplatelets are at higher risk of worse outcomes than those not taking these drugs.

Table 3. Results of the high risk subgroup studies (GreenLight 120-W treatment) anticoagulant/antiplatelet groups

Outcome measure	Treatment	Woo 2008	Woo 2011
IPSS (mean (SD))	Anticoagulant/ antiplatelet	8.6 (4.3) (n=53) -62.4%	10.6 (7.2) (baseline 23.3 (6.1))
	None	7.9 (4.5) (n=163) -64.7%	NR
QoL (mean (SD))	Anticoagulant/ antiplatelet	NR	2.1 (2.0) (baseline 4.8 (0.98))

	None	NR	NR
Qmax (mean (SD))	Anticoagulant/ antiplatelet	18.7 (9.4) (n=53) +128.0%	17.5 (7.2) (baseline 7.2 (2.8))
	None	22.0 (10.1) (n=154) +214.3%	NR
PVR (mean (SD))	Anticoagulant/ antiplatelet	56.0 (75.1) (n=57) -78.5%	51.0 (52.0) (baseline 226 (172))
	None	30.7 (49.2) (n=182) -88.0%	NR
Prostate volume (mean (SD))	Anticoagulant/ antiplatelet	35.8 (16.2) (n=42) -50.8%	NR
	None	32.5 (17.4) (n=118) -44.2%	NR
NR – not reported			

High risk subgroups – larger prostates

Woo (2008) compared outcome results at mean follow up of 4.2 months for participants with larger v smaller prostates (see Table 4). There is insufficient information on whether patients with larger prostates are at higher risk of worse outcomes than those with smaller prostates.

Table 4. Results of the high risk subgroup studies (GreenLight 120-W treatment) larger vs smaller prostate groups

Outcome measure	Prostate size	Woo 2008 (n, % change from baseline)
IPSS (mean (SD))	Prostate size ≥80ml	8.0 (4.8) (n=45) (-63.6%)
	Prostate size <80ml	8.1 (4.4) (n=167) (-64.2%)
Qmax (mean (SD))	Prostate size ≥80ml	19.7 (9.1) (n=44) (+233.3%)
	Prostate size <80ml	21.7 (10.3) (n=158) (+185.5%)
PVR (mean (SD))	Prostate size ≥80ml	40.6 (71.9) (n=47) (-86.4%)

	Prostate size <80ml	35.0 (52.6) (n=181) (-85.9%)
Prostate volume (mean (SD))	Prostate size ≥80ml	55.5 (18.1)# (n=31) (-52.5%)
	Prostate size <80ml	28.1 (12.0)# (n=128) (-42.3%)
# p<0.001		

High risk subgroups – patients in urinary retention

Woo 2011 reports the results for IPSS, QoL, Qmax and PVR in a subgroup analysis of men in and not in urinary retention at presentation. This found that there were significantly worse IPSS symptoms at 3 months follow up in patients not in urinary retention compared to those who were. There were no significant differences in the three other outcome measures.

Woo 2008 also reported IPSS, QoL, Qmax and PVR subgroup results according to baseline urinary retention status. This found that there were significantly better Qmax scores at an average of 4.2 months follow up in the patients not in retention at baseline and no differences in the other three outcomes.

3.7 Description of the adverse events reported by the sponsor

The sponsor reported the adverse events described in the GOLIATH Trial (Thomas 2015) and made general points about the safety of laser use in the operating theatre. The EAC queried the MAUDE database and found descriptions of expected adverse events of incontinence, dysuria, retrograde ejaculation, haematuria, urinary tract infection, bladder neck contracture, and capsular or bladder perforation.

In the GOLIATH trial the adverse events were reported by Clavien-Dindo Grade (Dindo 2004). See Appendix 1 for a description of the Clavien-Dindo grades. There were 117 adverse events in 71 patients in the GreenLight 180-W group compared to 98 adverse events in 62 patients in the TURP group by six months (according to Bachmann 2014). The description of the adverse events for Thomas (2015) contradicts these numbers, suggesting that at 6 months there were 112 adverse events in 69 patients with GreenLight 180-W treatment compared to 100 adverse events in 64 patients with TURP. In months 7-12 the relevant numbers for GreenLight 180-W treatment and TURP were 14 in 12 patients and 5 in 5 patients, and at months 13-24 they were 5 in 5 patients and 2 in 2 patients respectively. At 6 months there were more grade I and II adverse events in the GreenLight 180-W group compared to the TURP group whereas there were more IIIa and IIIb adverse events in the TURP group compared to the GreenLight 180-W group but none of the totals

was statistically significant (Bachmann 2014). The numbers of events were too low to see any trends between 6-24 months follow up. Similarly, numbers of events for bleeding at the different Clavien-Dindo grades were too low to see any trends between GreenLight 180-W treatment and TURP. TUR syndrome and capsular perforation rates were not reported in any of the 3 GOLIATH publications.

High risk subgroups - anticoagulants and/or antiplatelets

Chung 2012 had 44% of patients taking anticoagulants and/or antiplatelets. . Patients who continued to take at least one antiplatelet/anticoagulant medication had an 11% risk of experiencing a bleeding-related complication, compared with patients who were not taking antiplatelet/anticoagulant medications who had a 4% risk of experiencing a bleeding-related complication.

In Woo 2011, 15 adverse events were reported and the paper mentioned that 'almost a third of patients had an adverse event'. As 15/43 =35% it is likely that one patient had more than one adverse event. There were 2 patients (4.7%) that had prolonged haematuria and 1 had readmission with a secondary bleeding episode. There were no blood transfusions required.

In Woo 2008 there were a number of peri-operative and postoperative early complications reported for the anticoagulant/antiplatelet group compared to patients not taking these drugs. The relevant haemostatic results between the two groups were the need for electrocautery to control bleeding (anticoagulant/antiplatelet group 1.5%, none 2.9%) and the need for blood transfusion within 12 weeks (anticoagulant/antiplatelet group 1.5%, none 0%). Levels of significance were not reported for these outcomes.

High risk subgroups – large prostates

In Woo 2008 there were a number of peri-operative and postoperative early complications reported for the large prostate group (>80g) compared to patients with smaller prostates.

Table 5. Woo 2008 peri-operative and postoperative early complications in patients with larger versus smaller prostates

Outcome	Prostate size <80ml	Prostate size ≥80ml
Need for electrocautery to control bleeding	2.1% (5/235)	3.8% (2/52)
Capsular perforation	1.3% (3/235)	0
Early dysuria	14.6% (30/235)	9.6% (5/52)

Recatheterisation	5.1% (12/235)	3.8% (2/52)
Urinary tract infection	4.7% (11/235)	3.8% (2/52)
Dysuria (severe)	2.5% (6/235)	0
Blood transfusion	0.4% (1/235)	1.9% (1/52)
Urinary incontinence	0.9% (2/235)	0
Reoperation (insufficient voiding)	0.9% (2/235)	0
Urethral stricture	0.4% (1/235)	0
Bladder neck stricture	0.4% (1/235)	0

There is insufficient information to determine whether there are more or fewer adverse events with GreenLight 180-W treatment than TURP because the sample size of the single trial available is insufficient to demonstrate any differences.

From the submitted evidence by the sponsor there is insufficient information to determine whether adverse events are more likely with GreenLight 120-W treatment than HoLEP in patients taking anticoagulant/antiplatelet medication, or with larger prostates, and no evidence on other high risk subgroups.

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

There was no evidence synthesis or meta-analysis conducted by the sponsor and this would have been inappropriate, given the amount of evidence found in the primary searches (1 RCT) and the study designs in the secondary searches (case series). The sponsor however referred to a systematic review and meta-analysis performed by Bachmann et al (2012). A critical appraisal of this review of prostatectomy evidence from twenty five recent RCTs on BHP indicates it is a narrative review. There is no description of it being a systematic review or a meta-analysis (the paper does not contain a meta-analysis). There is no statement of search terms used to find included studies and no description of inclusion criteria. Therefore it is impossible to know whether the included studies are representative of the total body of evidence available or not. Also, it only looks at GreenLight 80-W and 120-W treatment and lists 5 RCTs comparing these to TURP. Therefore it is not useful for the evaluation of GreenLight 180-W treatment compared to TURP.

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

1. Additional searches were conducted in Medline (Ovid), Embase (Ovid) and Central (Cochrane Library). Searches were conducted on 6th and 7th October 2015 and relevant text-files downloaded. Search terms were a mixture of appropriate MESH terms and textwords for BPO and GreenLight laser treatment. GreenLight synonyms included pvp, photoselective vaporization, 180-W and XPS. The searches were scanned by one reviewer for additional includeable studies, using the inclusion criteria in the NICE final scope.

2. Analysis of the additional studies found evaluating GreenLight 120-W laser in patients with BPO taking antiplatelets and/or anticoagulants.

3. Analysis of the additional studies found evaluating GreenLight 180-W laser in patients with BPO and larger prostates.

4. Critical appraisal of the RCT of GreenLight 180-W vapo-enucleation vs HoLEP (Elshal 2015)

5. Comparative review of 180-W vs 120-W GreenLight treatment (see Appendix 3)

6. Critical appraisal of a recent systematic review of HoLEP vs TURP

7. Critical appraisal of an additional RCT of GreenLight 180-W vs TURP (Jovanovic 2014)

8. Critical appraisal of GreenLight 120-W vaporisation vs HoLEP RCT (Elmansy 2012)

Analysis of additional studies found evaluating GreenLight 120-W laser in high-risk patients

Anticoagulant and/or antiplatelet use

No studies using the GreenLight 180-W system in patients on anticoagulants and/or antiplatelets were found in the EAC searches. Table 2 gives details of the 6 additional studies published in English on patients with BPO at high risk, using the 120-W GreenLight laser (Cakiroglu 2013, Chen 2013a, Chen 2013b, Sohn 2011, Tam 2012 and Tao 2013) that were found during the searches. The comparative studies (Chen 2013b, Sohn 2011, Tao 2013) give more useful information than the case series without comparators (Cakiroglu 2013, Chen 2013a, Tam 2012) so the results of the comparative studies are presented here. A non-comparative case series published in French (Bouabdallah 2013) was also found but is not reported here.

The RCT of the strategy of continuing or discontinuing anti-coagulants (Sohn 2011) had a small sample size of 30 in each group so may not have been powered to find relatively small differences in outcomes. It was described as a 'retrospective randomised study' and the meaning of this statement is difficult to discern. The mean total operation time (SD) in the stopped anticoagulant group was 24.9 (12.4) minutes compared to 16.9 (6.1) in the continuing medication group. There was no significant difference between the two groups in the haemoglobin change from before to after the operation. There were no significant differences in IPSS, QoL score, PVR and prothrombin time at baseline or at 3 month's follow up. None of the patients in either group developed haematuria, infections or other complications.

The two comparative case series (Chen 2013b, Tao 2013) had relatively small numbers of patients on anticoagulants or anti-platelets compared to the total numbers in the cohorts. Chen 2013b examined several subgroups of patients (age >80 years, larger prostate, high anaesthetic risk, anticoagulant risk) and a comparison was made between anticoagulant use patients and those with no high risk factors. Tao 2013 gave results for the subgroup on anticoagulants and the whole cohort (including the subgroup on anticoagulants). Therefore the results between the two studies are not comparable, because the comparators were different.

For Chen 2013b, the mean hospital stay (SD) was 2.3 (1.0) days in the anticoagulant group and 1.7 (1.2) in the no high risk factor group. There was no significant difference in IPSS, QoL, Qmax and PVR for the anticoagulant group compared to the no high risk factor group. No patients were given blood transfusions and one patient in the anticoagulant group had delayed haematuria requiring intervention compared to none in the no high risk factor group. There were significantly more urinary tract infections in the anticoagulant group (3 vs 1). There were no other noticeable differences between the two groups in postoperative complications.

For Tao 2013 the mean (SD operation time for the anticoagulant group was 49.5 (14.8) minutes compared to 50.8 (15.5) for the whole group. The mean (SD) postoperative haemoglobin for the anticoagulant group was 13.4 (1.0) compared to 13.4 (1.2) for the whole group. None of the follow up results were given for the anticoagulant group separately.

Larger prostates

Table 3 gives details of the four additional studies found on patients with BPO with larger prostates, using the 180-W GreenLight laser (Altay 2015, Hueber 2015, Nicholson 2015, West 2014). Altay 2015 and Nicholson 2015 do not give comparative results but Hueber 2015 and West 2014 give the results of treatment according to prostate size. In Hueber 2015 it is greater than 80ml

(n=387) or lesser than 80ml (n=741) and for West 2014 it is <40ml (n=27), 40-79ml (n=56), 80-119 ml (n=38), >120ml (n=22).

In Hueber 2015 the mean prostate size per group was not given. The median (IQR) length of hospital stay in hours was 24 (19) in the lesser than 80ml group and 24 (18) in the greater than 80ml group. The median (IQR) total operative time in minutes was 45 (25) and 80 (62) respectively. The number of Clavien-Dindo complications > grade 2 were 84 and occurred in 11.4% of patients and 62 and occurred in 16.0% of patients respectively. The rate of capsular perforation was 0.5% and 0.9% respectively and no patients required blood transfusions in either group. Significantly more patients in the larger prostate group required conversion to TURP (0.6% vs 8.4%). IPSS, QoL, Qmax, PVR and PSA results for the two subgroups at baseline, 6 months, 12 months and 24 months were reported. At baseline, the IPSS, PVR and PSA scores were significantly lower in the lesser than 80ml group and the Qmax were significantly more in the lesser than 80ml group. At 6 months, only the PSA scores were significantly lower in the lesser than 80ml group. At 12 months The IPSS scores were significantly higher in the in the lesser than 80ml group and the PVR and PSA scores were significantly lower in this group. At 24 months only PVR and PSA scores were significantly lower in the lesser than 80ml group and there was no difference in IPSS scores between the two subgroups.

In West 2014 the mean (SD) prostate volume in cc in each group was 29 (11), 59.5 (16.5), 91.5 (17.5) and 142.5 (48). The mean (SD) length of hospital stay was 20 (4.5), 19 (5.25), 20.5 (6.75) and 20 (15.5) hours respectively. The mean (SD) operation time was 34 (14.5), 50.5 (22.25), 75 (23.25) and 109.5 (43.25) minutes respectively. The number of Clavien-Dindo complications > grade 2 were 1, 3, 4 and 3 respectively and the number anticoagulated were 4, 5, 10 and 5 respectively. None of these results were statistically significant. No follow up outcomes were reported.

Table 6. Details of the 6 additional studies on high risk patients (all received GreenLight 120-W laser treatment)

Study	Patient population	Country	Age	Study design	Sample size
Cakiroglu 2013	Men with BPO secondary to BPH, and on anti-coagulants. Recruited between 2007-2010	Turkey	Mean age 72.8 yrs, (range 65-89)	Retrospective case series with follow up at 3 months	63
Chen 2013a	Men with LUTS due to BHP, at high risk including on anticoagulation, having CVD, liver or kidney dysfunction, respiratory disease or diabetes mellitus. Recruited between 2009-2011	China	Mean age 82.8 years (range 70-96)	Prospective cohort study with follow up to 24 months.	120
Chen 2013b	Subgroups of case series of patients with LUTS associated with BPH with large prostates (>80 ml) and/or on anti-coagulants. Recruited between 2008-2010	Taiwan	Total sample mean age not given. Subgroup results suggest mean age ~70 yrs.	Retrospective case series with follow up at 1, 12 and 24 months	Total sample size 132, 21 on anti-coagulants,
Sohn 2011	Patients with LUTS from BHP who were taking anticoagulants because of CVD. Recruited between 2009-2010	South Korea	Total sample mean age not given. Subgroup results suggest mean age ~69 yrs.	RCT randomised to continuing or discontinuing anti-coagulants. Follow up to 3 months	60, (30 in each arm).
Tam 2012	Patients with LUTS from BHP who had a bleeding tendency or were taking anticoagulants or antiplatelets. Recruited between 2007-2010	Hong Kong	Mean age 76 (range 62-94)	Prospective case series with follow up at 1,3,6 and 12 months	48

Study	Patient population	Country	Age	Study design	Sample size
Tao 2013	Patients with LUTS from BHP who had cardiopulmonary disease and a subgroup taking long-term anticoagulants. Recruited between 2007-2009	China	Mean age 72.7 (SD 4.7)	Prospective case series with follow up at 1,3,6 and 12 months	Total sample size 188, 45 on anticoagulants

Table 7. Details of the additional study on patients with large prostates

Study	Patient population	Country	Age	Study design	Sample size
Altay 2015	Consecutive patients with LUTS due to BHP. All had prostates larger than 80mL. Recruited between 2011-2013	Turkey	Mean age 71.1 (range 49-85)	Prospective cohort with follow up to 12 months.	68
Hueber 2015	Patients with BPH with a subgroup analysis based on prostate size. Recruited between 2011-2012	6 centres in Canada, France, UK, USA	Median age 70 (IQR 13)	Prospective cohort with follow up at 6, 12 and 24 months.	Total sample size 1196, 387 with larger prostates
Nicholson 2015	Patients with bladder outflow obstruction from BPH, with prostates larger than 100mL. Recruited between 2010-2013.	Australia	median age 70 (interquartile range [IQR] 66-79)	Prospective cohort with follow up at 3 and 6 months	35
West 2015	Patients with LUTS from BPH, with a subgroup analysis based on prostate size	Australia	Mean age 68.0, (SD 10.1)	Retrospective case series with time point at surgery	Total sample size 137, 60 with larger prostates

Critical appraisal of the RCTs of GreenLight 180-W vapo-enucleation vs HoLEP (Elshal 2015) and GreenLight 120-W vaporisation vs HoLEP (Elmansy 2012)

Elshal 2015 is an RCT of GreenLight 180-W vapo-enucleation v HoLEP in patients with LUTS secondary to BPH. It reports peri-operative parameters, standard outcome measures and adverse events of the two treatments.

It was not included in the Sponsor's submission because the technique used is vapo-enucleation rather than vaporisation so the technique is different to that being evaluated in the Sponsor's submission and has been described by the manufacturer as off-label use of the equipment. The technique includes some blunt dissection of the prostate before using the GreenLight laser to dissect the lobes of the prostate. There is no mention of a morcellator being used, unlike the description of the HoLEP treatment where a morcellator was used. The technique described in the clinical trials database (NCT01494337) was that: Both HoLEPand GreenLight XPS laser vaporization of the prostate begins with the insertion of a resectoscope transurethrally. Examination of the lower urinary tract is performed and holmium laser fiber is used to enucleate (HOLEP) or to vaporize (GreenLight XPS) the obstructing prostatic tissue using MoXy fibre until the surgical capsule is reached. In the publication (Elshal 2015) the technique is described as being similar to thulium laser vapo-enucleation of the prostate. They used blunt dissection of the adenoma to locate the prostatic capsule then progressively more power (80-W to 180-W) from the GreenLight 180-W laser to enucleate some of the tissue and vaporise other parts in order to achieve a TURP-like cavity.

However, this RCT has been discussed here as it is the only direct evidence available comparing GreenLight 180-W to HoLEP treatment, which is the comparison being evaluated in high risk subgroups of patients. (NB no case series were found of GreenLight (180-W) vaporisation compared to HoLEP).

In the RCT there were 53 patients in the GreenLight 180-W group and 50 in the HoLEP group. The results of the RCT are given in Table 8. For most of the peri-operative and follow up outcomes at 12 months there was little difference between the two groups. However, more patients in the GreenLight group required a hospital stay of more than 1 night due to haematuria (6 vs 3 cases) and due to medical concern (6 vs 0 cases).

Randomisation was achieved through computer-generated random tables. Patients were stratified block randomised according to size (40-80ml and >80ml) and catheterised vs non-catheterised. There is no mention of allocation concealment. There is no mention of blinding of the investigator (all procedures were performed by a single surgeon) or outcomes assessors. A description of losses to follow up are given and are reasonably balanced,

except that 4 patients in the HoLEP group and none in the GreenLight 180-W group were found to have prostate cancer. There was no sample size calculation mentioned. The statistical analysis was appropriate to the outcomes.

Table 8. Results of RCT of GreenLight 180-W vapo-enucleation vs HoLEP

Measure	GreenLight 180-W	HoLEP	P values
Mean age (SD)	74.1 (8.8)	71.0 (9.3)	0.09
Mean (SD) operating time (mins)	103 (35)	114 (35)	0.1
Mean (SD) haemoglobin deficit (g/dl)	0.74 (1.1)	0.74 (0.82)	0.9
Mean (SD) hospital stay (days)	1.5 (1.3)	1.1 (0.7)	0.055
Hospital stay of more than one night	23.5%	6.4%	0.02
Capsule violation	5.6%	2%	0.61
Anaemia requiring transfusion	1.8%	0	1*
Postop haematuria	3.7%	2%	1*
IPSS (mean (SD)) (estimated from graph)	5 (4.5)	4 (6)	NG
QoL (mean (SD)) (estimated from graph)	1 (1.2)	0.9 (1.3)	NG
Qmax (mean (SD)) (ml)	18.5 (7.0)	31.1 (14.0)	P=0.01
PVR (mean (SD)) (estimated from graph)	70 (90)	50 (50)	NG
Grade IIIa Clavien Dindo AEs by 1 year	6%	7.4%	NG
* p values as given in paper but may be incorrect			

Elmansy 2012 is an RCT of GreenLight 120-W vaporisation v HoLEP in patients with LUTS secondary to BPH. It reports peri-operative parameters, standard outcome measures at 3 months, 6 months and 12 months, and adverse events of the two treatments. Randomisation was achieved using a number generator computer programme. There was no mention of allocation concealment or blinding of outcome measures. However, intention-to-treat analysis was used, so the 8 GreenLight 120-W patients who converted to TURP were included in the GreenLight 120-W group.

In the RCT there were 37 patients in the GreenLight 120-W group and 43 in the HoLEP group. The mean (SD) operation time in the GreenLight 120-W group was 110 (41.5) and in the HoLEP group was 107 (35.1). There were 2 patients who needed retreatment for residual adenoma in the GreenLight 120-W group compared to none in the HoLEP group. The 8 people who converted from GreenLight 120-W treatment to TURP were because of bleeding causing impaired operative vision, failure to control bleeding or inadequate tissue removal. IPSS, QoL, Qmax, and PVR outcomes at follow up are reported. For IPSS there were no significant differences between the two groups at follow up. For QoL the scores were higher for the HoLEP group at 1 and 3 months but not at 6 months or 12 months. For Qmax, the HoLEP group had higher scores at all follow ups and for PVR the HoLEP group had lower scores at all follow ups.

Comparative review of 180-W vs 120-W GreenLight treatment

This review is in Appendix 3. It shows that the operating time and mean hospital stay tends to be longer with the 120-W laser compared to the 180-W laser. More fibres tend to be used with the 120-W laser compared to the 180-W laser and there is a slightly lower risk of capsular perforation with the 120-W laser compared to the 180-W laser. At follow up there seem to be few consistent differences between the two lasers but the numbers of events were low for both treatments.

Meta-analysis of the operating time was conducted in Revman (version 5.2) using a random effects model. Standard deviations were calculated from ranges where necessary using the standard approximation of dividing the range by 6 (as 99% of values are +/- 3 standard deviations). The results are approximate because of this calculation but show that GreenLight 180-W laser treatment took significantly less operating time than GreenLight 120-W treatment – mean difference 16.87 (95% confidence intervals 7.61 to 26.14) (see Figure 5).

Critical appraisal of a recent systematic review of HoLEP vs TURP

The most recent systematic review of HoLEP vs TURP is by Li et al (2014). This included patients with BHP and meta-analysed the standard outcome measures reported in the included RCTs of IPSS, Qmax, PVR and intra-operative complications. It addressed an important clinical question and included the correct types of studies. The search strategy was appropriate and comprehensive. Double inclusions and data extraction were performed and results summarised appropriately. Eight RCTs contributed to the meta-analyses, reported in 15 papers.

The numerical results from the meta-analyses are given in Table 9. They show that HoLEP operations take longer than TURP but the hospital stay is shorter. There are few differences in postoperative complications (those non-statistically significant are not reported here but include TUR syndrome, mucosa injury, acute urinary retention, urinary tract infection, transient haematuria, urethral stricture, urinary incontinence, transient dysuria and bladder neck stenosis. HoLEP has statistically significantly better curative outcomes at follow up.

Table 9. Meta-analysis results from HoLEP vs TURP systematic review

Outcome		Weighted mean difference (95% CIs)	Direction of effect
Duration of operation		14.19 (6.30 to 22.08)	Favours TURP
Length of hospital stay (hours)		-22.25 (-29.81 to -20.68)	Favours HoLEP
IPSS	3 months	0.47 (-0.98 to 1.92)	NA
	6 months	-0.61 (-0.36 to 0.14)	NA
	12 months	-1.17 (-1.99 to -0.34)	Favours HoLEP
Qmax	3 months	3.49 (0.64 to 6.35	Favours HoLEP
	6 months	0.62 (-0.70 to 1.94)	NA
	12 months	1.47 (0.40 to 2.54)	Favours HoLEP
PVR	6 months	-8.90 (-15.15 to -2.64)	Favours HoLEP
	12 months	-15.98 (-22.50 to -9.47)	Favours HoLEP
Intraoperative complications	Blood transfusions	0.17 (0.06 to 0.47)	Favours TURP
	Secondary treatment	0.57 (0.31 to 1.05)	Favours HoLEP

Critical appraisal of RCT of GreenLight 180-W treatment vs TURP.

This small RCT (Jovanovic 2014) enrolled 62 patients with LUTS due to BPH and 31 were treated with GreenLight 180-W and 31 with TURP. Patients were recruited from hospital in Serbia between 2011 and 2013. The inclusion criteria were patients with moderate or severe LUTS (IPSS score > 16), failure of previous medical treatment, Qmax <15ml/s, PVR >100ml, PV <100ml and ability to give consent. Excluded were patients on anticoagulants, with urethral strictures, bladder stone or neurogenic bladders, or suspected of having

prostate cancer. Follow up was at 1,3,6 and 12 months but only intra-operative and postoperative outcomes and adverse events reported.

It was stated to be a randomised trial but method of randomisation was not given. There was no information on allocation concealment or blinding of outcome measurement. There is no information on withdrawals or drop-outs during treatment or losses to follow up.

The median age of participants was 66.3 in the GreenLight 180-W group and 67.1 in the TURP group. No information was given on ethnicity. The mean (SD) operation time in minutes was 92 (18) and 82 (13) respectively and the mean hospital stay in days was 1.9 (0,8) and 4.4 (0.6) respectively. With regard to adverse events, 0 patients in the GreenLight 180-W group had blood transfusion, capsule perforation or TUR syndrome whereas in the TURP group there were 6 patients with blood transfusions, 5 with capsule perforation and 1 with TUR syndrome. These results were statistically significantly different. Postoperatively, the IPSS scores were 5.2 and 4.8 and the Qmax scores were 18.7 and 18.5 respectively.

3.10 Conclusions on the clinical evidence

Four studies were submitted by the sponsor, one RCT of GreenLight 180-W vaporisation vs TURP (the GOLIATH RCT) for the main indication and 3 case series for high-risk subgroups. The RCT was of high quality but the case series were of lower quality and 1 was irrelevant as there were insufficient high-risk participants included. Searches by the EAC revealed an additional 10 case series for high risk groups, of which 3 yielded useful comparative information. The EAC also found an RCT of GreenLight 180-W vapo-enucleation vs HoLEP. Although this use of GreenLight 180-W is off-label, it is the only evidence available at the moment for any use of GreenLight treatment compared with the comparator appropriate to high risk subgroups (HoLEP).

The submitted evidence for the non-high risk population reflected the decision problem in that it presented good evidence available from an RCT that included appropriate patients. The intervention in the RCT was the latest version of GreenLight laser treatment (180-W) and an appropriate comparator was used (TURP). The clinical outcomes reported in the GOLIATH RCT were appropriate and included operation time, post-operative catheterisation, hospital length of stay, IPSS, Qmax, PVR, prostate volume, QoL, complications and numbers of retreatments.

The submitted evidence for high risk populations partially reflected the decision problem in that it provided evidence from 3 of the 12 case series available. Only 1 of the 4 comparative case series available was included in the sponsor's submission. The patients in the case series were poorly described but probably appropriate. The interventions were GreenLight 120-W for the evidence on patients taking anticoagulants and 180-W for the evidence in patients with larger prostates. There was no comparative evidence of GreenLight laser treatment vs HoLEP.

There is sufficient information to suggest that GreenLight 180-W treatment is clinically similar in effectiveness and adverse events than TURP. The operating time is longer for GreenLight 180-W treatment so it is likely that fewer cases will be treated if no additional operating theatre list time is available. However, as catherisation time and hospital stay are shorter with GreenLight 180-W than with TURP, indicating post-operative recovery is quicker, there may be scope for more efficient hospital bed use with GreenLight 180-W than with TURP.

In high risk subgroups the comparative case series for patients on anticoagulants and with larger vs smaller prostates had sample sizes too small to show any noticeable differences in effectiveness or adverse events. In the RCT of GreenLight 180-W using an off-label technique compared to HoLEP, there may be slightly more bleeding episodes with GreenLight 180-W treatment but this result was not statistically significant, possibly due to small sample sizes. The RCT on 120-W treatment also suggested more bleeding episodes with GreenLight 120-W compared to HoLEP because of the numbers of the GreenLight 120-W patients who crossed to TURP. The GreenLight HPS 120-W system however is an older generation of GreenLight laser and technical differences between the GreenLight 120-W HPS system and the GreenLight 180-W XPS system may result in different outcomes, including rate and volume of tissue removal, and the ability to coagulate bleeding vessels. Numbers of events in the comparative review of the GreenLight 180-W XPS system and the GreenLight 120-W HPS system were low, precluding firm conclusions. Therefore, in the high risk subgroups there is insufficient information to know whether there is equivalent operation times, effectiveness or similar rates of adverse events with GreenLight 180-W treatment in patients taking anticoagulation treatment, with larger vs smaller prostates compared to HoLEP or in patients presenting with or without urinary retention.

4 Economic evidence

4.1 Published economic evidence

Critique of the sponsor's search strategy

The search strategy used by the sponsor to identify relevant economic studies was described in section 10.3 Appendix 3 in the sponsor's submission. The searches were conducted on 18 Sept 2015. The key words used includes a strategy that combined (GreenLight OR XPS OR 180-W or 180-W or 180-watt) AND (prostate OR prostatic OR BPH) AND (cost or costs or economics). A time filter (01/01/2010 – 31/12/2015) was applied to coincide with the introduction of the GreenLight XPS 180-W version in 2010. The databases used were Medline, Embase, MEDLINE (R) In-Process, EconLit and NHS EED.

The EAC ran its own search on Ovid Medline and Embase with slightly different syntax but using the same search terms. No further relevant studies were identified.

The sponsors did not do any formal searches to identify resource measurement and valuation.

Critique of the sponsors study selection

The inclusion criteria were broadly consistent with the scope and were largely the same as those used to evaluate clinical studies, except for the study designs and outcomes (costs or cost-effectiveness analyses). The inclusion criteria restricted papers published in English language only and those that evaluated a specific model of the GreenLight laser (i.e. XPS 180-W).

The EAC did not identify any major economic study missed by the Sponsor's selection criteria.

Included and excluded studies

The Sponsor included two studies- Thomas et al. (2015) based on GOLIATH trial and Benejam-Gual et al. (2014) based on a multi-centre trial in Spain. Of the 25 studies identified via their searches, they excluded 23 as none of them evaluated the specific model of the GreenLight used in average risk patients (i.e. XPS 180-W). Table 10 summarises the main characteristics of the relevant included economic studies (Thomas et al 2015, Benejam-Gual et al 2014a).

Table 10. Cost effectiveness study included in economic study review

Study	Population	Intervention	Comparator	Costs and resource use	Comment
Thomas et al. (2015)	Patients with benign prostatic obstruction when medical therapy fails. The data included in the study come from 9 European countries (UK, Germany, France, Italy, Netherlands, Spain, Belgium, Austria, Switzerland)	PVP (GreenLight XPS 180-W)	TURP	• Procedure costs • Costs of complications • Quality of life (utilities) A state-transition Markov-type model with a lifelong time horizon was used. Various sources of data have been utilised to provide robust estimates of cost-effectiveness.	Several issues with the correctness of the input parameters used (see the section below). Omission of capital costs from the analysis makes the findings relevant to those contexts/situations only where no capital costs are actually incurred in adopting the technology. Sensitivity analyses shows mixed picture. Authors themselves advise to use caution in using the findings. One of the most relevant trial data used in the study (GOLIATH) found the costs were almost equal but if PVP led more than 32% patients undergoing PVP discharged as a day case in the UK context, it became cost-saving. Therefore, the main driver of the cost-effectiveness appears to be the proportion of cases that could be carried out as the day case.

Study	Population	Intervention	Comparator	Costs and resource use	Comment
Benejam-Gual et al. 2014a	Patients who were operated sequentially between July 2012 and October 2012 in 3 Spanish hospitals. To be included, the patient needed to have previous diagnosis of LUTS secondary to BPH, IPSS≥15, Qmax ≤15ml/sec and prostatic volume between 40 and 80ml. Patients with lack of floow up and lack of values in relevant variables were excluded.	PVP (GreenLight XPS 180-W)	TURP	Costs were identified and analysed in three phases – pre-surgical, surgical and post-surgical. Only direct medical care costs were included. This was achieved by counting quantities of resource use in each phase and multiplying that by relevant unit costs.	Not enough details on how resources were collected and valued. 2/4 hospitals had length of hospital stay ≤1 day for all patients treated with GL XPS 180-W. The average length of stay of 1.31 days is substantially shorter than that observed in the GOLIATH trial (Bachmann et al 2014). The exclusion criteria coupled with forced statistical methods (trimmed averages) yielded very small standard errors around the costs. It is legitimate to expect some patients to have longer lengths of stay but they were considered as “extreme values” that could just be “removed”.

No other relevant studies were identified by the EAC. No studies that were identified by the sponsor were excluded by the EAC

Overview of methodologies of all included economic studies

There was one relevant included study (Thomas et al. 2015). The EAC conducted its own critical appraisal on the study applying the Drummond and Jefferson (1996) checklist (see Appendix 4), the same checklist used by the Sponsor in Table 10, p. 49 of the submission.

Thomas 2015 aimed to assess the cost-effectiveness of GreenLight 180-W laser treatment when compared with the current standard for patients with

BPO when medical therapy has failed. The economic model and parameters used in this study came from the 2008 Health Technology Assessment (Lourenco et al. 2008).

The sponsor's model was a state-transition Markov-type model with a lifelong time horizon. Patients with symptoms of BPO were allowed to move to mutually exclusive states guided by their urinary and incontinence symptoms. Re-operations were allowed in case of insufficient relief but not in case of persistent urinary incontinence. Treatment was assumed not to affect mortality and the model used the age-specific population mortality rates for English men. To provide enough sensitivity, the model used five different data sources:

- A 2008 meta-analysis evaluating GreenLight 80-W laser treatment (Lourenco 2008). (A number of other data updates have been made since the Lourenco 2008 meta-analysis).
- A 2010 meta-analysis evaluating GreenLight 120-W laser treatment (NICE 2010)
- A Bayesian posterior estimate of 180-W effectiveness based on prior experience of GreenLight 120-W laser treatment and informed by GreenLight 80-W treatment
- The results of the GOLIATH RCT (180-W)
- A Bayesian posterior estimate informed by the GOLIATH RCT results (180-W)

Note that a Baysian approach to random effects meta-analyses was used to arrive at some of these estimates.

A few issues in the study that were missed in the Sponsor's critical appraisal are worth noting.

1. The risk ratios used in the model (based in the 2008 meta-analysis from Lourenco (2008) and presented in Table 10 of the sponsor's submission) for incontinence, blood transfusion, TUR syndrome and UTI do not match those presented in the HTA by Lourenco et al (2008). An error seems to have been made when Armstrong et al (2009) evaluated the cost-effectiveness of surgical treatments for men with BPE and used the data from Lourenco et al (2008) for GreenLight 80-W treatment. It seems that the authors used the GreenLight 80-W data presented in Armstrong et al (2009) for the model.

2. The procedure cost for GreenLight laser treatment is unclear as Thomas 2015 did not include the cost of the machine (Table 2 in Thomas et al. 2015); only the cost per MoXy fibre that would be used with GreenLight 180-W treatment was included. Previous economic evaluations of GreenLight 120-W (Benejam-Gual et al 2014b; Whitty et al 2013) – although not included in this review - estimated the capital costs of equipment and training costs for GreenLight 120-W treatment but it is not apparent if such costs were included in the Thomas et al (2015) paper. Additionally, the number of fibres used for GreenLight laser treatment per patient may vary, having been estimated at a mean (SD) of 1.38 (0.61) fibres/patient for 120-W treatment (Whitty et al 2013). The difference in number of fibres needed per patient for 180-W treatment does not seem to have been taken into account in the Thomas et al (2015) model.

3. The probability of requiring re-operation after GreenLight 120-W treatment as compared with TURP used in the Whitty et al (2013) model was based on a meta-analysis by Thangasamy et al (2012) which has also been used in the Thomas et al (2015) study. The risk ratios (95% CI) presented in Thangasamy et al (2012) for reoperation were 1.87 (0.65–5.39), but are reported in Thomas et al (2015) as 1.62 (0.56-372).

4. The authors of Thomas 2015 suggest that more than 70% of the patients with GreenLight 180-W treatment in the UK required less than 24 hours to achieve stable health and therefore could be treated as day cases. However, the median length of hospital stay for GreenLight 180-W treatment in the GOLIATH RCT was 49.3 hours (Bachmann et al 2014) and the reasons for the UK patients requiring less time is unclear. Judging by Figure 2 in Thomas et al (2015) there were more patients as day case with TURP than with GreenLight 180-W treatment, therefore invalidating the Thomas et al's (2015) assumptions, at least for the overall patient population. Note, however, that Figure 2 was based on data from all 9 European countries, where practice variation may be substantial.

Based on the above weaknesses, Thomas 2015's conclusions need to be interpreted with caution. Although it is unclear if the errors identified could have an impact in the results of the study, the apparent omission of capital costs would increase the costs of GreenLight 180-W treatment and therefore decrease the probability of GreenLight 180-W treatment being cost-effective when compared with TURP. In Thomas (2015), therefore, the main driver of the cost-effectiveness – subject to potential errors in the use of input

parameters as above- appeared to be the proportion of cases that could be carried out as day cases.

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

The results presented in the Thomas et al. (2015) indicated that there may be potential for GreenLight XPS 180-W treatment to generate cost-savings compared to TURP in average risk patients. However, there are issues with the way data were used, and the sensitivity analysis showed a mixed picture, indicating that the costs were probably the same as that of TURP. In the absence of full costing of the technology (i.e. exclusion of capital costs), the main driver of cost-savings, if any, would have been from a larger proportion in the GreenLight 180-W treatment group having been discharged as day cases compared to those treated with TURP. Thomas et al (2015) suggest this proportion to be at least 32%.

Despite all these weaknesses, Thomas et al (2015) remains the only relevant economic study to inform the Sponsor's model, particularly when GOLIATH RCT results are used. Benjam-Gual et al (2014a) study was not used in any explicit way to inform the Sponsor's model (9.1.1 p. 54 of the Submission) although it can be argued that the study implication was used as a supplementary evidence to Thomas et al. (2015) to design the Sponsor cost model, i.e. cost-saving might come from the shorter length of stays in GreenLight XPS compared to TURP. However, it is important to note that any conclusions based on the available economic evidence may still be subject to significant uncertainty. This is even more apparent when the target population is at high risk, as the GOLIATH RCT was based on an average risk population.

4.2 De novo cost analysis

The sponsor conducted a cost analysis based on data from GOLIATH trial and other sources to assess potential cost saving associated with use of GreenLight XPS 180-W laser surgical procedure in men with LUTS due to BPE. The cost analysis was conducted relative to two alternative procedures: (i) monopolar or bipolar TURP for average risk patients, defined as those with prostate volume <100ml, not in urinary retention and not on active anticoagulation therapy; or (ii) HoLEP for high risk patients, defined as those with large glands (>100ml), in urinary retention and/or on anti-coagulant therapy. The analysis was conducted to reflect GreenLight laser treatment use in a hospital setting.

The potential cost-saving was reflected mostly by expected differences in hospital length of stay and expected differences in treatment of post-surgery complications for a patient undergoing GreenLight 180-W treatment compared with TURP. No capital costs to adopt the technology was included in the analysis, as it was assumed that the console will be provided to the NHS free of charge if minimum fibre purchase is met (for GreenLight 180-W) and UK hospitals had the necessary capital equipment in place for TURP.

The sponsor produced a quantitative *de novo* model operationalised in MS Excel. The model allowed cost savings to be estimated and a deterministic sensitivity analysis around parameters inputs to be conducted to assess uncertainty.

Patients

In the cost analysis, the sponsor defined the patient group into two risk categories:

(i) Men with lower urinary tract symptoms (LUTS) due to benign prostatic enlargement with prostate volume <100ml, not in urinary retention and not on active anticoagulation therapy (average risk group)

(ii) Men with lower urinary tract symptoms (LUTS) due to benign prostatic enlargement with large glands (>100ml), in urinary retention and/or on anti-coagulant therapy (high risk group)

For the average risk category, data regarding incidence and length of stay which populated the cost model came from Thomas (2015) based on the GOLIATH trial outcomes. It is therefore relevant to assess how well the population in the GOLIATH trial fitted that defined in the scope.

The GOLIATH trial included men aged 40-80 years, with LUTS due to BPE who had a prostate volume less than 100 ml and who were not on active anticoagulation therapy. Participants had to have an IPSS score greater than or equal to 12 measured at the baseline visit, medical record documentation of Qmax < 15 ml/s and PV ≤ 100 ml by transrectal ultrasound (TRUS), classified American Society of Anaesthesiologists I, II or III, and a serum creatinine that was within the normal range for the study centre. Patients were recruited in 9 countries in Europe including the UK.

For the high risk category, however, additional data were used from Woo et al. (2008) on risk of bleeding. The Woo et al. (2008) study was a case series of patients with LUTS associated with BPH using EAU or AUA criteria with large prostates (>80 ml) and/or on anti-coagulants. All received GreenLight

120-W laser treatment and the study included patients from 6 countries including England (see Table 3 and Table 4).

In the GOLIATH RCT, the mean prostate volume in the GreenLight 180-W group and the TURP group were respectively 48.6 ml (SD=19.2) and 46.2 ml (SD=19.1). The population in GOLIATH trial therefore seems to broadly fit the population defined in the scope for average risk patients but not for high risk patients.

Technology

The technology was the GreenLight XPS 180-W laser system used in standard NHS clinical practice settings in hospitals.

Comparator(s)

The comparators were monopolar or bipolar TURP for average risk patients, and HoLEP for high risk patients, currently used in standard NHS clinical practice.

The model treated monopolar and bipolar TURP as a single intervention, assuming the same proportion (50% each) of patients needing TURP could be allocated to either monopolar or bipolar TURP. The opinions of clinical experts approached by the EAC suggested that all surgeons should now be using bipolar TURP but that this is not the case in practice currently in the NHS. The TURis MTG23 (NICE 2015) has recognised that the evidence demonstrated the clinical equivalence of bipolar (TURis) and monopolar TURP for prostatic resection.. However, there was a small difference in costs between monopolar and bipolar TURP due to additional consumables used in bipolar TURP.

Model structure

The Sponsor's chosen model structure reflected mostly the GOLIATH trial data (additionally Woo et al. 2008 for high risk patients), and was operationalised as a decision tree with four potential pathways. The Sponsor highlighted that this pathway was consistent with European Urology Association guidelines for the management of non-neurogenic male LUTS including BPO.

Upon surgical indication, patients could either undergo GreenLight XPS 180-W or TURP (average risk patient model) or HoLEP (high risk patient model).

The four pathways considered in the model were:

1. Operated and discharged after in-patient stay and had no further complications
2. Operated and discharged as a day case and had no further complications
3. Operated, discharged as in-patient and treated with post-surgery complications, either at Grade II or Grade III (a/b) or mix of both
4. Operated, discharged as day case and treated with post-surgery complications, either at Grade II or Grade III (a/b) or mix of both

Although the Sponsors included a flowchart diagram showing the patient pathways, it was not clear how post-surgery complications were being operationalised by the model. In particular, no distinction between severity of post-surgery complications (Grade II or IIIa/b or mixed, as suggested by GOLIATH trial – Bachmann et al. 2013) were made explicit. The model also assumed that complications were mutually exclusive and that no patient would have had more than one adverse events. This was clarified with the Sponsor by the EAC with the result that the Sponsor submitted an additional model 2 weeks after the initial model, with the ability for patients to have more than one adverse event. The original model has been analysed by the EAC.

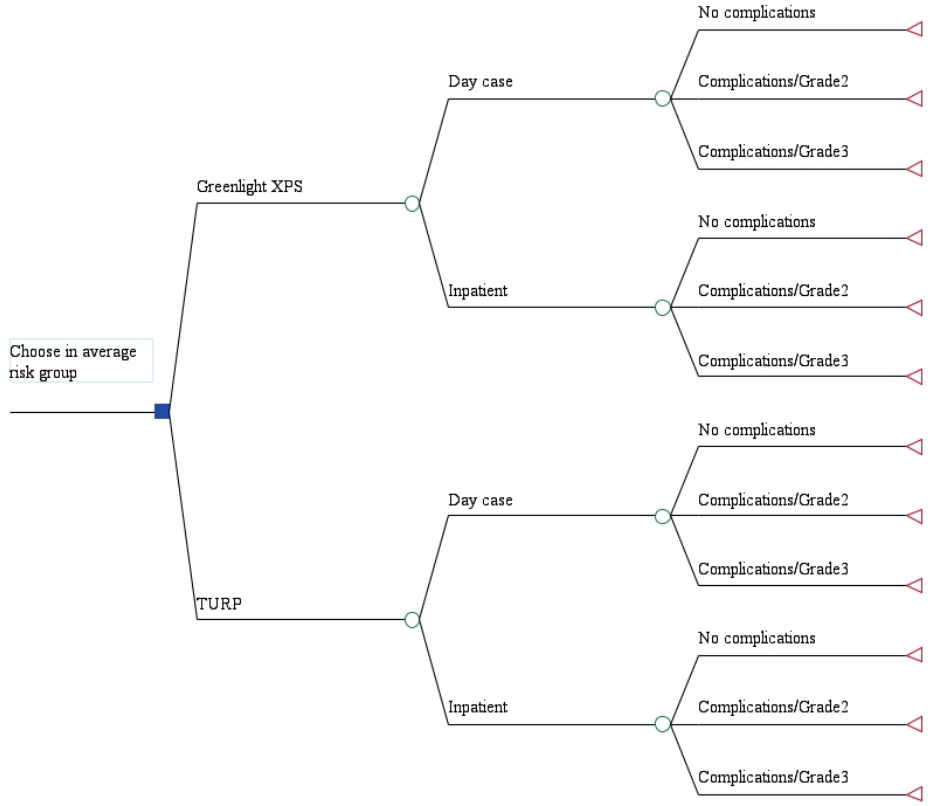
The EAC has re-drawn the flowchart to aid clarity (see Figure 2), showing possible pathways for a patient who undergoes surgery. Note that this was a simplified depiction of what might happen if a proportion of patients developed post-surgery complications. As Bachmann et al. (2013) reported from the GOLIATH RCT data that there was no significant difference in the incidence of adverse events between XPS and TURP, the EAC concluded that inclusion of additional branches in the decision tree to show three adverse events outcomes (no complications, complications requiring primary care, and complications requiring hospital stays) was therefore reasonable as a simplified approach.

The probabilities with which the patient may have moved into each pathway were sourced from GOLIATH trial data (Bachmann et al. 2013; Thomas et al. 2015) and other data provided in the Sponsor's submission. In Figure 2 a square represents a decision node, a circle represents a chance node and triangles represent terminal nodes. The only decision node in the model reflected the decision to undergo GreenLight 180-W or TURP (HoLEP in the high risk groups). This is further discussed in section 4.5.

The end-point of the model was 6 months after surgery, as it was assumed by the Sponsor, based on expert opinion, that any adverse events typically occurred within the first 6 months and based on GOLIATH data, adverse events were stable and similar between the two groups after six months (Bachmann 2014). In the Sponsor's model, costs for each group were

estimated based on cost per day of hospital stay (allowing for excess bed day costs) and other costs associated with the technologies.

Figure 2. Redrawn diagram of Sponsor's model – Patient pathways



A number of key assumptions were made in the Sponsor's model (listed in Table 11 of p. 55 of the Sponsor submission). In particular, a proportion of patients were expected to return home on the same day (day case) and, given uncertainty in this data, the Sponsor provided four different sources- Hospital Episode Statistics (HES); UK real-life data; French real-life data; and US Medicare data. As the main cost-driver in the model was length of stay, the final results may be sensitive to the source used for these data.

For the high risk group, the model inherently assumed that GreenLight 180-W would have the same safety and efficacy outcomes as HoLEP, justifying this assumption on the grounds of unavailability of any head-to-head comparative evidence.

The EAC identified an RCT (Elshal 2015) comparing GreenLight 180-W vapo-enucleation vs HoLEP in patients with LUTS secondary to BPH. The EAC believes that this study is the only evidence available comparing the two on

outcomes for high-risk groups, despite the technique being vapo-enucleation rather than vaporisation (see critical appraisal of Elshal 2015 in section 3.9).

It is understandable why the model structure was chosen, given the aggregated data to populate it from GOLIATH trial, and the underlying assumption that the major cost-drivers were the hospital length of stay.

Clinical parameters and variables

Most clinical parameters were sourced from a single study – the GOLIATH trial. Two key parameters (% treated inpatient and excess bed days) were however sourced from HES data. Table 11 provides a summary of the values used in the model for the base case analysis.

Table 11. Base case key clinical parameters used in the Sponsor's model

Parameters	XPS	TURP	HoLEP	Source
Proportion of patients undergoing surgery discharged as day case	35.96%	4.08%	35.96%	Sponsor analysed HES 2014-15 data
Mean excess bed days	10.36	10.65	10.36	Sponsor analysed HES 2014-15 data
IPSS at 6 months	6.80	5.60		Bachman et al (2014)- 6 month outcome in GOLIATH
% complication free at 6 months	87.31%	83.21%		Bachman et al (2014)- 6 month outcome in GOLIATH
% adverse event (example: non-acute UTI, a Grade II event treated in primary care)	14.71%	7.64%	14.71% (assumed similar to XPS)	Bachman et al (2014)- 6 month outcome in GOLIATH

The perspective taken in the analysis was that of the UK NHS. The time horizon was taken as 6 months after surgery as most of the differences in outcomes were observed by that point. This seems reasonable.

The EAC would draw particular attention to the following parameters:

a. If it was currently standard practice to offer GreenLight 180-W treatment to average risk patients in the UK, the use of HES data in identifying the proportion that would be discharged as a day case following surgery is appropriate. However, this is not the case and in their submission the Sponsor have acknowledged - based on their clinical experts' opinion following real-life data coming out from France, US and a high-volume XPS centre in England – that this proportion might be much lower than what would be feasible in standard practice. The Sponsor has provided alternative data from the above sources which can be used for sensitivity analysis. However, it would be appropriate to check that with data from GOLIATH trial itself (all countries vs. UK only). Upon request, the Sponsors provided this data to the EAC to be used as academic in confidence material (see section 4.5).

b. A key parameter in the model is average length of hospital stay. The Sponsor's model dichotomised all inpatients as either <5 days or >5 days and applied excess bed days to those who stayed longer than 5 days. Whilst most clinical data came from the GOLIATH trial, the model did not use mean LOS data from the trial itself (65.5 hours in XPS vs 96.9 hours in TURP). The EAC explored whether appropriate 'per day' costs could be applied to make use of this robust data. However, the only available cost for this purpose is the 'excess bed days' which would be applicable only when inpatient stays are longer than the trim point for this HRG (5 days in this case). In other words, if length of stay for most of the patients were longer than 5 days, applying excess bed day costs as a proxy to 'per day' tariff would have been appropriate but the GOLIATH trial data on lengths of stay indicated otherwise. Therefore, EAC agreed with the Sponsor model approach to apply mean reference cost for most of inpatients assuming they would stay in the hospital for less than 5 days.

c. Treatment of adverse event parameters in the model is not very clear. One assumption that the Sponsor model made is the mutual exclusivity of adverse events (i.e. no possibility for a patient to develop more than one complication allowed). Upon query by the EAC, the Sponsor confirmed that this was the case in their original model justifying on the ground that they expected a small overlap in patients experiencing multiple events, and sent a revised model since (not evaluated by

EAC) in which they claimed to have accounted for any such overlap. Based on the GOLIATH data (Bachmann et al. 2013), the EAC worked out a simplified way in which average number of adverse events (acute or non-acute) per patient could be entered to the model to take into account the likelihood of multiple adverse events (see further work done by EAC).

d. Since the extent to which the data on average risk group could be transferable to high risk group is not clear, the EAC would draw particular attention to the usage of GOLIATH trial data in evaluating cost-savings between XPS and HoLEP.

e. The GreenLight XPS 180-W procedure takes on average about 10 minutes longer than TURP procedure, a statistically significant difference observed in GOLIATH trial (Bachmann 2013). Therefore, it is likely that fewer cases will be treated if no additional operating theatre list time is available. This opportunity cost has not been taken into account by the Sponsor; rather they have assumed the operating time was expected to be similar with TURP justifying on two grounds: (i) GOLIATH trial might have learning curve bias; and (b) expert opinions of consultants who involve in both types of procedures in daily basis found no difference.

f. Quality of life changes were not included in the model explicitly. Whilst differences in IPSS score and percentage of patients who were symptom free were presented, they are not part of any direct cost analysis/comparison.

Resource identification, measurement and valuation

Although the sponsor mentioned that targeted searches were performed to identify most relevant NHS costs, the submission did not provide any details as to how that search helped them identify potentially relevant resource use. They seem to have consulted their Clinical Advisors and included economic study (Thomas et al. 2015) to seek some guidance. As the result, the sponsor consulted relevant national tariffs and NHS reference costs. The sponsor identified five key categories of resource use:

- **Hospital resources** to conduct the procedure, manage recovery, and follow up
- **Consumable**s
- **Treatment of adverse events** in hospital and/or primary care settings

- **Capital** costs (for HoLEP only)
- **Others** (the cost of continuous saline bladder irrigation in half of the TURP procedures only)

A summary of variables applied in the cost model is provided in Table 16, p.62 in the submission. The table is copied in

Table 12 below:

Table 12. Summary of variables applied in the cost model (copied from the Sponsor's submission

Variable	Value	Range or 95% CI (distribution)	Source
Unit cost per day case procedure	£1,544.00	£1,235.20 - £1,852.80 (Varied by 20.0%)	PbR Tariff LB25F
Unit cost per inpatient procedure	£2,485.00	£1,988.00 - £2,982.00 (Varied by 20.0%)	PbR Tariff LB25F
Unit cost per outpatient visits	£101.00	£80.80 - £121.20 (Varied by 20.0%)	NHS Reference Cost for Outpatient Attendances: Service Code 101 - Urology
Unit cost per excess bed day	£294.00	£235.20 - £352.80 (Varied by 20.0%)	PbR Tariff LB25F
Total cost of consumables per PVP surgery	£550.00	£440.00 - £660.00 (Varied by 20.0%)	Thomas et al, Value in Health 2015
Total cost of consumables per TURP surgery	£145.16	£116.13 - £174.19 (Varied by 20.0%	Expert opinion
Total cost of consumables per HoLEP surgery	£[redacted]	£[redacted] - £[redacted] (Varied by 20.0%)	Boston Scientific UK Internal Sales Data
HoLEP Console	£[redacted]	£[redacted] - £[redacted] (Varied by 20.0%)	Boston Scientific UK Internal Sales Data
Morcellator Console	£30,000	£24,000 - £36,000 (Varied by 20.0%)	Expert opinion
Patients Treated per Hospital per Year	25	20 – 30 (Varied by 20.0%)	Expert opinion
Useful Life (years)	5	4 – 6 (Varied by 20.0%)	Expert opinion
Depreciation Rate	3.5%	2.8% - 4.2% (Varied by 20.0%)	Expert opinion

HoLEP capital cost per procedure	£[redacted]	£[redacted] - £[redacted] (Varied by 20.0%)	Boston Scientific UK Internal Sales Data
Unit cost of Incontinence event - moderate	£147.06	£117.65 - £176.48 (Varied by 20.0%)	NICE CG97 2010 Appendices A-H, costs inflated to 2015; PSSRU 2015
Unit cost of urinary retention event - Non-acute	£48.77	£39.02 - £58.52 (Varied by 20.0%)	NICE CG97 2010 Appendices A-H, costs inflated to 2015; PSSRU 2015; BNF 2015A; Expert Opinion
Unit urinary retention event - Acute	£1,238.63	£990.91 - £1,486.36 (Varied by 20.0%)	HRGs LB16E and LB16F – weighted average based on activity and unit cost
Unit cost of bleeding event - Non-acute	£47.31	£37.8 - £56.77 (Varied by 20.0%)	PSSRU 2015; BNF 2015A; Expert Opinion
Unit cost of bleeding event - Acute	£849.42	£679.54 - £1,019.30 (Varied by 20.0%)	HRG LB14Z – weighted average of day case and non-elective inpatient short stay
Unit cost of stricture event - Acute	£1,201.55	£961.24 - £1,441.86 (Varied by 20.0%)	HRG LB29A – weighted average of day case and non-elective inpatient short stay
Unit cost of UTI event	£47.13	£37.70 - £56.56 (Varied by 20.0%)	Turner et. al, 2010[17]
% of TURP patients that have bladder irrigation	50%	40% - 60% (Varied by 20.0%)	Expert opinion

Unit cost of saline irrigation per surgery with TURP	£45.34	£36.27 - £54.41 (Varied by 20.0%)	NHS Price list 2015 and Expert Opinion
PVP - mean excess bed days amongst patients who stay >5 days where an excess bed day charge is applied	10.36 days	8.288 - 12.432 days (Varied by 20.0%)	NHS HES data 2014-2015
TURP - mean excess bed days amongst patients who stay >5 days where an excess bed day charge is applied	10.65 days	8.52 - 12.8 days (Varied by 20.0%)	NHS HES data 2014-2015
HoLEP - mean excess bed days amongst patients who stay >5 days where an excess bed day charge is applied	10.36 days	8.288 - 12.432 days (Varied by 20.0%)	NHS HES data 2014-2015; HES data does not differentiate between laser type, therefore, value is the same as for GreenLight

As one can see from

Table 12, the Sponsor's model took into account a large number of cost parameters. Whilst the ones highlighted (in green) were the Sponsor's own estimates, other data were sourced from the public domain or, where no data were available; estimates were obtained based on expert opinion.

A unit cost of £101 was applied to all patients as it was assumed that all patients would need one consultant-led outpatient visit. The data were sourced from the 2013/14 Reference Cost schedule (NHS 2014), consultant-led outpatients (urology). The Reference Costs schedule was also used to source unit costs for day case, inpatient stay and excess bed days.

A weighted average approach was used to obtain the average costs of treating non-acute adverse events using the Healthcare Resource Group (HRG) codes. For example, the HRG code "LB14Z Intermediate Endoscopic Bladder Procedures" for Day Case and Non-elective Inpatients (short stay) was used to estimate the unit cost of acute bleeding event ((£849.42) by applying observed number of activities in the schedule as the weight.

A bottom-up approach was used to cost the consumables, acute events and others, first identifying ingredients and valuing those to add up to the unit costs. For example, to cost mono-polar TURP, the following ingredients would be needed: 1 mono-polar TURP loop, 4 bags of 2L glycine used during the procedure and 1 Ellik evacuator for chip removal. The appropriate average costs to value those resources were taken from relevant published and/or unpublished sources.

Capital costs were considered only for HoLEP, assuming GreenLight 180-W lasers were to be provided to the NHS hospitals on long-term loan with a minimum number of MoXy fibres purchased per year. The Sponsor's main submission (p.57) and accompanying model technical document (p. 17) have conflicting messages whether the fibre cost (£550) would include the costs of acquiring the equipment including maintenance. Looking further at their cost model, the EAC assumed that it would. MoXyThe £550 MoXy fibre costs came directly from Thomas et al. (2015), whose original source was the HTA 2008 report (Lourenco 2008) that specified single-use fibre costs in HoLEP machines (not XPS 180-W) to be between £550 and £750 per patient. However, fibres used in 80-W and 120-W GreenLight treatment are different to those used in 180-W treatment so the costs will be different.

The TURP device was assumed to be already present in the NHS hospitals, i.e. no financial costs were assumed to incur in the use of TURP. This assumption made the opportunity costs of capital investment on any existing TURP device to equal zero. This may be a problematic assumption, particularly if GreenLight 180-W consumables (MoXy fibre costs) included the opportunity costs of using the GreenLight 180-W device.

If £550 did not include the rental/lease costs of using GreenLight 180-W, assuming zero capital costs for both makes sense but there is uncertainty around hospitals' ability to purchase a minimum number of fibres per year to hold the capital costs at zero.

The EAC therefore assumed - for this assessment purpose - that GreenLight MoXy fibre will be available to the NHS hospitals at £550 per surgery and the GreenLight XPS 180-W console free of charge.

The HoLEP capital equipment required to conduct a procedure consisted of a laser and a morcellator. The Sponsor's internal market data on the unit cost of four HoLEP laser types was used to obtain the per-patient capital costs of using HoLEP (£[redacted]). The equipment's amortised period was assumed to be 5 years, with a rate of 3.5%, and the number of high risk patients expected to be treated per hospital with HoLEP per year was assumed to be 25. The cost (£[redacted]/surgery) is therefore a 'mortgage' payment needed to be paid by the hospitals to be able to use the equipment for 5 years.

Technology and comparators' costs

The Sponsor provided the list price of the GreenLight XPS 180-W console at £[redacted] and consumables (MoXy fibre) at £[redacted]. However, the sponsors state clearly that these higher prices are seldom used when selling to hospitals. Instead, they assumed the console price to be zero and the MoXy fibre price at £550 [redacted].

Table 13 has the summary of technology and comparator costs:

Table 13. Technology and comparator costs

GreenLight XPS 180-W	TURP	HoLEP
Capital: £0 Consumables = £550/surgery	Capital =£0 Consumables = £190.50/surgery	Capital = £[redacted]/surgery Consumables= £[redacted]/surgery

Sensitivity analysis

The Sponsor's model was implemented as a simple decision tree owing to the 6 month time horizon and is a fair representation of current clinical practice. As such, the Sponsor opted to conduct a deterministic sensitivity analysis in which each model input was varied one at a time to recalculate the net difference in costs per patient between the two technologies. A lower and

higher value was chosen for each parameter (

Table 12). The clinical inputs were varied with two values - the upper and lower limits of a 95% distribution assuming a beta distribution. All cost inputs were varied by an arbitrary 20% in each direction. The results were presented on a tornado plot (see

Figure 3) which shows the range around the values that had the greatest impact on the results.

Because of the way the cost-savings were implemented in the model, the results were highly sensitive to a single parameter – the proportion of cases who would be discharged on the same day (day case) following the GreenLight 180-W procedure. The sponsor acknowledged on p.69 of the submission that huge uncertainty existed around this figure. Therefore, the model was constructed to allow a scenario analysis in which users could choose one of the following four figures for the proportion of day cases:

a. Rate of a day case from one UK hospital (80%)

b. Rate of day case taken from HES data (35.96%)

c. Rate taken from the French NHS data (57.71%)

d. Rate taken from the US Medicare patient population (71.50%)

The EAC understands that this parameter is a major source of uncertainty in the model and therefore would plot cost-savings against the entire spectrum (0-100%) to estimate the threshold at which GreenLight becomes cost-saving. This will be revisited in section 4.5.

4.3 Results of de novo cost analysis

The results are presented for average risk patients and under all four scenarios. The cost-saving is the net difference in costs between GreenLight XPS 180-W procedure and TURP and presented as ‘per patient’.

Base-case analysis results

Table 14 shows the Sponsor's model base case results.

Table 14. Sponsor's model base case results

	Cost per average risk patient		Cost-saving per average risk patient*
	GreenLight XPS	**TURP**	
Procedure cost	£ 2,284.88	£ 2,637.46	£ 352.58
Consumables	£ 550.00	£ 145.16	-£ 404.84
Non-Acute events	£ 15.84	£ 11.54	-£ 4.30
Acute events	£ 108.11	£ 147.99	£ 39.88
Capital	£ -	£ -	£ -
Other	£ -	£ 45.34	£ 45.34
Total	**£ 2,958.83**	**£ 2,987.48**	**£ 28.66****

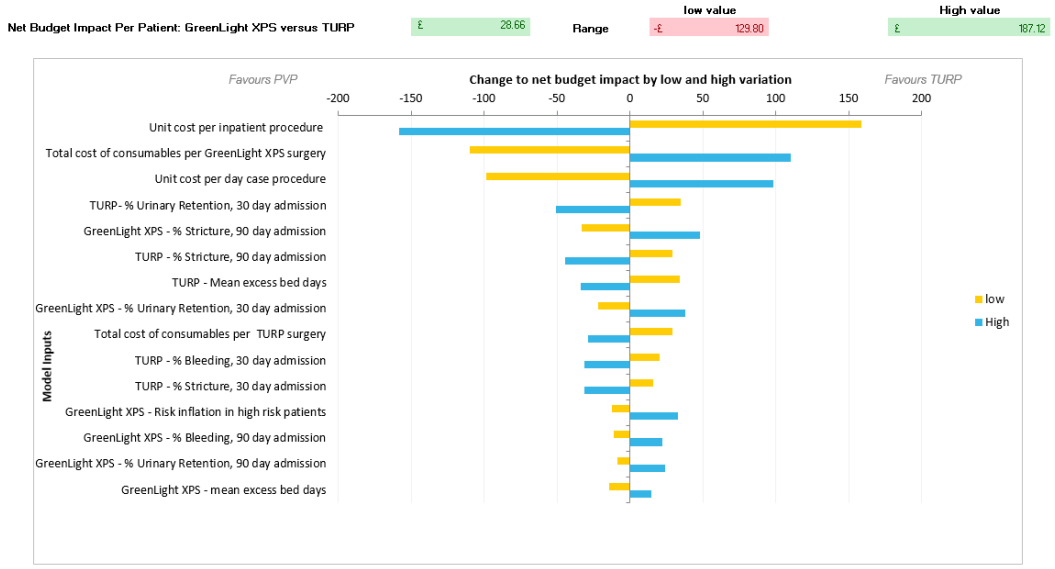
* A minus sign indicates GreenLight XPS is more expensive in this cost category.
** £443 (using single UK hospital day case rate); £233 (using French day case rate); £363 (using US day case rate)

Sensitivity analysis results

Given the day case rate of 35.96% (fixed in the analysis), the Sponsor's sensitivity analysis using other input parameters showed that unit costs for inpatient procedures, the consumable cost for PVP and the unit costs for outpatient procedures were the first three parameters having the greatest impact on the results (see

Figure 3). A 20% change in the unit cost of inpatient procedures in either direction, for example, resulted in the net difference in cost between GreenLight 180-W and TURP between -£129 (GreenLight 180-W more expensive) and £187 (TURP more expensive). The Sponsor interpreted this result as GreenLight XPS 180-W being expected to be cost-neutral compared TURP.

Figure 3. Tornado plot from sensitivity analysis



When the day case rate was varied and the deterministic sensitivity analysis was repeated using the same parameters as above, the parameter that had the greatest impact on the results was still the unit cost per inpatient procedure. However, the cost of consumables moved down to third place and the unit cost of day case procedure up to the second place, when the proportion of day cases following GreenLight 180-W was increased to reflect other sources of data. The Sponsor concluded that GreenLight 180-W treatment is cost-saving compared to TURP if day case rate following GreenLight 180-W treatment is similar to the rates observed in France, the US or the single UK hospital.

The sensitivity analyses thus confirmed that the modelled cost savings were most sensitive to the length of stay values (day case or inpatient stays) used.

Subgroup analysis

Subgroup analysis was carried out by the Sponsor for ‘high risk’ patients, defined as those who were suffering from LUTS due to BPO or BPH. They were the patients in urinary retention, on anti-coagulation therapy or with a large prostate gland >100 ml as defined in the project scope. The Sponsor’s submission made it clear that identification of this subgroup was consistent with European Urologic Association guidelines. TURP was considered an inappropriate therapy for these patients and HoLEP was presented as an alternative procedure.

The same economic model was then used to model the cost-savings from GreenLight XPS compared to HoLEP with following key changes:

a. On grounds of absence of comparable data, both safety and efficacy outcomes in HoLEP were assumed to be similar to GreenLight 180-W treatment (Woo et al. 2008, which used GreenLight 120-W treatment)
b. Capital cost was introduced in the calculation of HoLEP costs
c. All adverse events were treated as similar to average risk patients (Bachmann 2013), except for bleeds of all types (from Woo et al. 2008).

The base case results were presented as the cost-saving per high risk patient (see Table 15).

Table 15. Base case results from Sponsor's model, high risk patients

	GreenLight XPS	HoLEP	Difference
Procedure cost	£ 2,284.88	£ 2,284.88	£ -
Consumables	£ 550.00	£ [redacted]	-£ [redacted]
Non-Acute events	£ 16.55	£ 16.55	£ -
Acute events	£ 133.59	£ 133.59	£ -
Capital	£ -	£ [redacted]	£ [redacted]
Total	**£ 2,985.02**	**3,836.15**	**£ 851.13**

Note that the cost saving in Table 15 is the result of difference in consumable and capital costs only, as the Sponsor's model assumed all other clinical parameters to be the same in both groups. Although the sensitivity analysis in Sponsor's model confirmed that cost savings were likely to be between £591 and £1059 in favour of GreenLight 180-W, the input parameters that had the greatest effect were now capital cost elements. The unit costs of inpatients and day cases were still important drivers of uncertainty but not to the extent of the capital cost elements.

Model validation

The sponsor verified that they designed the model to emulate clinical pathways derived through consultation with expert clinical advisors and from the EAU LUTS Guidelines. The modelling was operationalised in MS Excel and all cells containing variables were named to facilitate checking.

The EAC checked codes in the modelling independently. In addition, the EAC ran a series of simple verification checks to assess the model for errors. This involved manipulating parameters and observing the outcomes of modelling, to ensure the model behaved in line with expectations. The series of checks

confirmed the computational consistency of the models and showed no major errors. The following checks were conducted:

- All costs were set to £0 except GreenLight XPS consumables costs and ensured additional costs were equal to cost of GreenLight XPS consumables.

- With all other costs set to £0 the number of uses per GreenLight increased by multiples to ensure consistency.

- Percentage treated as inpatient and day case as well as percentage staying longer than 5 days and mean excess bed days in GreenLight XPS was replicated in TURP, to ensure that there were no differences in procedure cost, under these parameter inputs.

Reassured by these simple checks, the EAC then conducted a thorough investigation of each worksheet and cells, to ensure calculations were accurate, and found no major errors. The Sponsor was consulted to verify some minor issues that were picked up during validation.

4.4 Interpretation of economic evidence

The Sponsor noted that their results were in line with the conclusion made by Thomas et al. (2015), the only relevant economic study. They interpreted the findings as costs of GreenLight XPS 180-W being comparable with current practice and under certain assumptions, GreenLight 180-W XPS treatment even had the potential to offer cost-saving to the NHS.

However, the cost savings resulted mostly from a couple of key assumptions: (a) that GreenLight XPS 180-W treatment led to much higher proportion of patients discharged on the same day compared to current practice; and (b) GreenLight XPS 180-W consoles can be acquired by the NHS at no capital cost as long as a minimum number of consumables (MoXy fibres) were purchased. This will be discussed further in Section 4.5 below.

On high risk patients, since all clinical parameters in HoLEP are assumed to be the same as that in GreenLight 180-W the Sponsor's conclusion about GreenLight 180-W being cost-saving stems from higher capital costs of HoLEP compared to zero capital costs of GreenLight under the same assumption as above.

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

The EAC reviewed studies evaluating the costs of GreenLight 80-W and 120-W models and the results all suggested that GreenLight laser treatment at these powers was either less costly or had the same cost with similar effectiveness as in TURP (Whelan et al 2013; Whitty et al 2014; Benejam-Gual et al 2014b). In the Armstrong et al (2009) study, GreenLight 80-W treatment was unlikely to be cost-effective in their model; the GreenLight 80-W data was based on the Lourenco et al 2008 meta-analysis.

The EAC verified the sponsor's search strategies for economic studies by conducting independent searches. The EAC produced its own critical appraisal of the Thomas et al. (2015) paper on which the sponsor's submission is based (Table 24. Quality assessment of health economic study).

The EAC validated the sponsor's economic model and reconstructed decision tree for clarity as well as validity check (Figure 2. Redrawn diagram of Sponsor's model – Patient pathways. This reconstruction was based on the response by the Sponsor on EAC's questions as well as first hand observation (arranged kindly by the Sponsor) of the use of GreenLight 180-W treatment in a clinical setting, and subsequent discussions with the performing clinician by two members of the EAC.

The EAC version of the model used the mean inpatient day costs, as Figure 2 in the Thomas et al (2015) study suggested that the long tail (requiring excess bed days) were very similar in GreenLight 180-W and TURP. In addition, cost-savings were evaluated against the entire spectrum of day case proportion (0-100%) to estimate the threshold at which GreenLight XPS 180-W becomes cost-saving. To do this, the rate of day cases in the TURP group was held at the current level.

To populate the model, it was necessary for the EAC to reanalyse some of the data from GOLIATH trial as some of Sponsor's assumptions around adverse events were not apparent from GOLIATH data reported in Bachmann et al. (2013). Sponsors were therefore requested to provide GOLIATH data for the EAC to reanalyse it but they confirmed this was not possible. Therefore, the EAC re-analysed adverse event data based on Bachmann et al. (2013). This reanalysis provided the EAC the following parameters:

Table 16. Model parameters re-estimated by EAC

Input parameters used	GreenLight XPS 180-W	TURP	Source
Proportion with post-surgery complications needing treatment at hospital (Grade 3)	19/136	27/133	Estimated by EAC based on Bachmann et al. (2013) Table 6
Number of post-surgery complications per patient who needed treatment at hospital (Grade 3)	32/30	21/19	Estimated by EAC based on Bachmann et al. (2013) Table 6
Proportion with post-surgery complications needing treatment at primary care (Grade 2)	30/136	19/133	Estimated by EAC based on Bachmann et al. (2013) Table 6
Number of post-surgery complications per patient who needed treatment at primary care (Grade 2)	19/19	29/27	Estimated by EAC based on Bachmann et al. (2013) Table 6
Average cost of treating adverse events in the hospital per patient	£937.82	£973.82	Weighted average of LB16E and LB16F non-elective admissions, intermediate bladder procedure, non-elective major open urethra procedures, outpatient urethra procedure
Average cost of treating adverse events in primary care per patient	£58.74	£47.27	Average of primary care costs in the Sponsor model weighted by proportion of such patients having specific adverse events from GOLIATH data (Bachmann 2013, Table 6)

As seen in Figure 2, the EAC simplified how the Sponsor treated the adverse events. As the primary data source (GOLIATH trial) suggested no significant difference in the incidence of adverse events between GreenLight 180-W and TURP for average risk patients, but that there was a small chance of multiple adverse events per patient, the EAC modelled this using the probability of having an adverse event that needed to be treated at primary care (Grade 2) or at the hospital (Grade 3), and the number of such events per patient over the 6 month period.

The unit cost of treating the adverse events in the hospital was revisited. A weighted average of the HRG procedures identified in the Sponsor model was used with the respective finished consultant episodes (FCE) from the Reference Cost schedule as the weights. This cost was then applied to the proportion of patients developing adverse events needed to be treated in the hospital times the number of adverse events per such patient to obtain the total cost of adverse events in GreenLight 180-W. A similar method was used to derive that cost in the TURP treatment group as well.

Thus, the EAC version of the economic model was produced by addressing a few issues with Sponsor's model raised in the previous sections. In particular, pathways to adverse events were simplified to allow for multiple events per patient, more appropriate average estimates of treating a typical adverse event in different settings (hospital and primary care) were used, and a refined version of the treatment pathway that is sensible for data availability used. In the sensitivity analysis, the threshold (of day case to inpatient ratio) after which GreenLight XPS becomes cost saving was estimated. The EAC decision tree is provided in Figure 2, p. 48.

Results of the EAC version of the model

The EAC version of the model estimated the base case cost-saving to be £60.19 per patient as opposed to the Sponsor's model (£28.66), assuming the day case rate in GreenLight 180-W to be 35.96% as observed in the HES data. The main difference in results between the EAC model and the Sponsor's model is the amount of adverse events related treatment costs. The direction of cost savings (positive or negative), though, remained the same between the two versions of the model.

Table 17: EAC average risk model results

	GreenLight 180-W	TURP	Difference
Day Case	£ 555.28	£ 63.00	-£ 492.28
Inpatient	£ 1,628.60	£ 2,473.46	£ 844.86
Grade 2 complications	£ 13.82	£ 7.46	-£ 6.36
Grade 3 complications	£ 131.02	£ 204.49	£ 73.47
Capital	£ -	£ -	£ -
Outpatient follow-up	£ 101.00	£ 101.00	
Consumables	£ 550.00	£ 145.16	-£ 404.84
Other	£ -	£ 45.34	£ 45.34
Total	**£ 2,979.72**	**£ 3,039.91**	£ 60.19

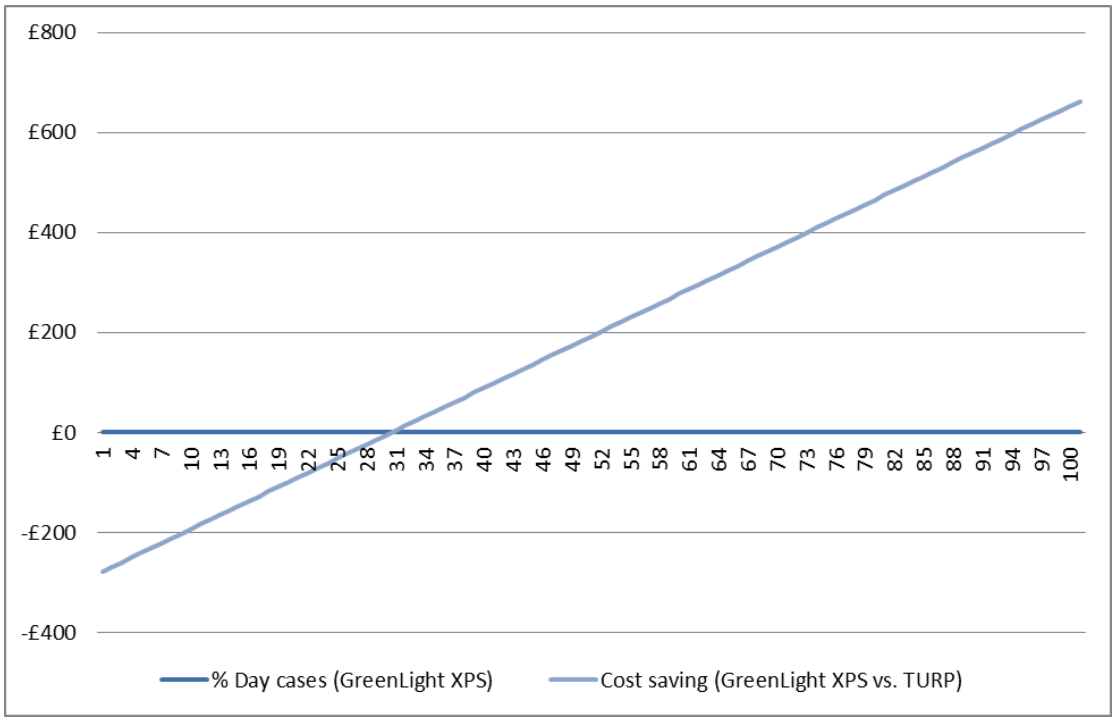
Since no further data on HoLEP in the format required by the EAC model was available, all clinical inputs between GreenLight and HoLEP were assumed to be similar. The EAC model on HoLEP thus replicated the results from the Sponsor's model.

It is important to reiterate that in the high risk subgroups there was insufficient information to know whether there is equivalent operation times, effectiveness or similar rates of adverse events with GreenLight 180-W treatment in patients taking anticoagulation treatment or with larger vs smaller prostates compared to HoLEP. Therefore, cost-savings in high risk population is still subject to considerable uncertainty which could not be evaluated in the absence of relevant data.

The sensitivity analysis on the most influential input parameter (proportion of patients discharged as day case) showed that in order for the GreenLight 180-W to be cost-saving against TURP in average risk patients, this proportion must be at least 30% (see Figure 4).

Upon request by the EAC, the Sponsor also provided day case rate observed specifically in the UK in the GOLIATH trial in academic confidence. [redacted].

Figure 4: Sensitivity of Day case-to-Inpatient ratio to cost-savings



As the EAC work has provided different results, see the 'Impact on the cost difference between the technology and comparator of additional clinical and economic analyses undertaken by the EAC' section.

4.6 Conclusions on the economic evidence

The sponsor's submission relied on data from a single RCT (GOLIATH trial) and appropriate national sources such as the Reference Costs and Hospital Episode Statistics. However, the main driver of the cost-saving was the proportion of patients discharged as day cases following GreenLight 180-W treatment. Currently, there is substantial uncertainty around this data and therefore the conclusion that GreenLight 180-W treatment is cost-saving is subject to this uncertainty.

Despite this, the EAC confirms that the sponsor's conclusion that GreenLight 180-W treatment may be cost saving is unaltered - the scale of savings is slightly higher though. However, this conclusion should be subject to: (a) at least 30% patients discharged as the day case following GreenLight 180-W treatment; and (b) NHS hospitals should be able to buy the minimum number of fibres so that the GreenLight 180-W console can be obtained free of charge.

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

The difference in the estimates of cost savings between sponsor's submission and the EAC version is reported in Table 18. The EAC models scale the savings up from the Sponsor's model in average risk patients. This reflects the fact that slightly more adverse events per patient occurred in TURP compared to the GreenLight 180-W treatment in the GOLIATH trial.

However, the Sponsor's conclusion that GreenLight 180-W treatment is cost-saving is unchanged, provided the day case to inpatient ratio in GreenLight 180-W is at least 30:70 and that NHS hospitals are able to buy the minimum number of fibres per year from the Sponsor.

Table 18. Variation in Sponsor and EAC estimates in average risk patients

Cost category	EAC base case estimates				Sponsor's base case estimates		
	GreenLight 180-W	TURP	Difference		GreenLight 180-W	TURP	Difference
Day Case	£ 555.28	£ 63.00	-£ 492.28				
Inpatient	£ 1,628.60	£ 2,473.46	£ 844.86				
Procedure (Day case, inpatient, outpatient)					£ 2,284.88	£ 2,637.46	£ 352.58
Grade 2 complications	£ 13.82	£ 7.46	-£ 6.36		£ 15.84	£ 11.54	-£ 4.30
Grade 3 complications	£ 131.02	£ 204.49	£ 73.47		£ 108.11	£ 147.99	£ 39.88
Capital	£ -	£ -	£ -				
Outpatient follow-up	£ 101.00	£ 101.00					
Consumables	£ 550.00	£ 145.16	-£ 404.84		£ 550.00	£ 145.16	-£ 404.84
Other	£ -	£ 45.34	£ 45.34		£ -	£ 45.34	£ 45.34
Total	**£ 2,979.72**	**£ 3,039.91**	£ 60.19				

Finally, the implications of longer procedure time for GreenLight XPS 180-W treatment compared to TURP of 49.6 (SD 21.8) minutes compared to 39.3 (SD 18.5) minutes for TURP patients, a statistically significant difference ($p<0.001$) – must be considered. Whilst the Sponsor states clearly on p. 15 and p. 76 of their submission that due to higher day case rates under the GreenLight XPS 180-W procedure, surgical urology inpatient beds will be freed up for other interventions. This might be true as long as at least 30% of average risk patients undergoing the GreenLight XPS procedure are discharged as day cases; otherwise the technology is more expensive. In addition, a 10 minute longer operating time for GreenLight 180-W treatment makes it likely that fewer cases will be treated if no additional operating theatre list time is available.

5 Conclusions

For average risk men with LUTs due to BPO, only one RCT was submitted in evidence compared to TURP and this was only powered to be a non-inferiority RCT. There is sufficient information to suggest that GreenLight 180-W treatment is clinically similar in effectiveness and adverse events than TURP. However, the operating time is longer for GreenLight 180-W treatment so it is likely that fewer cases will be treated if no additional operating theatre list time is available.

For high-risk men with LUTs due to BPO there were no RCTs available. The only evidence comes from small comparative case series. For patients taking anticoagulants no GreenLight 180-W case series were available and there was limited information from comparative case series using GreenLight 120-W treatment compared to HoLEP. For men with larger prostates, GreenLight 180-W limited information was available from comparative case series. Therefore, in the high risk subgroups there is insufficient information to know whether there is equivalent operation times, lengths of stay, effectiveness or similar rates of adverse events with GreenLight 180-W treatment in patients taking anticoagulation treatment or with larger vs smaller prostates compared to HoLEP.

The economic evidence on which the sponsor's submission is based (Bachmann 2013 and Thomas et al. 2015) is respectively randomised design and stochastic model and appropriate to use in such evaluations. As the main driver of cost saving is the proportion of patients discharged as the day case following GreenLight XPS and there exists significant uncertainty around this parameter, the cost-effectiveness modelling is not free from such an uncertainty. However, the EAC work suggests that GreenLight 180-W treatment can be cost-saving if the day case to inpatient ratio is at least 30:70

in average risk patient group and GreenLight XPS console is provided to NHS hospitals free of charge. No conclusion on cost-saving could be derived for high risk patient group in the absence of relevant data.

6 Implications for research

The effectiveness of GreenLight 180-W treatment is only shown in one RCT that was only powered to show non-inferiority with TURP. There is a strong need for a larger trial, adequately powered to demonstrated whether GreenLight 180-W treatment is more or less effective that TURP in average risk patients. There is no available evidence in the effectiveness of GreenLight 180-W vaporisation compared to HoLEP in high risk patients and RCTs in these patients are required.

Our understanding of the cost-effectiveness of GreenLight XPS will be improved by future studies that include quality of life and use more robust data on the proportion that could be discharged as the day case following a GreenLight XPS procedure. In addition, additional analysis from the GOLIATH trial providing data on average lengths of stay in patients with post-surgery complications by the type of adverse events would be helpful for the future economic evaluations. Finally, the differences in operating time between GreenLight XPS and TURP procedures in real-practice settings need to be investigated further to weigh up the opportunity costs involved.

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Appendices

Appendix 1. Measurement of BPH surgery outcomes - glossary

IPSS is The International Prostate Symptom Score. It is an 8 question (7 symptom questions + 1 quality of life question) written screening tool used to assess symptoms of BPH. The 7 symptoms questions include feeling of incomplete bladder emptying, frequency, intermittency, urgency, weak stream, straining and nocturia, each referring to during the last month, and each involving assignment of a score from 1 to 5 for a total of maximum 35 points. The 8th question of quality of life is assigned a score of 1 to 6. A total score of 0-7 is mildly symptomatic, 8-19 moderately symptomatic and 20-35 severely symptomatic.

Qmax is the maximum flow rate of urine and is a measure of the quantity of urine excreted in a specified period of time. Qmax is used as an indicator for the diagnosis of enlarged prostate. A lower Qmax may indicate that the enlarged prostate puts pressure on the urethra and a higher number indicates better functioning.

PVR is the post-void residual, ie the amount of urine left in the bladder after urinating. If there is an enlarged prostate which is affecting bladder function, the PVR will be higher.

PSA is prostate-specific antigen (also known as gamma-seminoprotein or kallikrein-3 (KLK3)), is a glycoprotein enzyme and is secreted by the epithelial cells of the prostate gland. It is present in small quantities in the serum of men with healthy prostates, but is often elevated in the presence of prostate cancer or other prostate disorders, including BPH and prostatitis. Only 30 percent of patients with high PSA have prostate cancer diagnosed after biopsy. The normal range of PSA without cancer rises with age. In men aged 60-69 it is 0.3 – 8.3 and in men aged 70 or over it is 0.4 – 17.8).

ICIQ-UI SF is a standardised self-report measure of urinary incontinence. It has 4 questions about how often and when urine leaks, the quantity of urine that leaks and how much it interferes with everyday life. It is scored from 0-21 with a higher number indicates more problems with incontinence.

IIEF-5 is a standardised self-report measure of erectile function. It has 5 questions on getting and maintaining an erection and sexual intercourse. It is scored from 5-25 where 5 is severe erectile dysfunction and 25 is no erectile dysfunction.

Clavien-Dindo grading is a standard surgical adverse event classification (Dindo 2004). Grade I is any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and

radiological interventions. Grade II is requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included. Grade III is requiring surgical, endoscopic or radiological intervention, Grade IIIa is intervention not under general anaesthesia, Grade IIIb is intervention under general anaesthesia. Grade 4 is life-threatening complication (including CNS complications) requiring intermediate care or intensive care unit management, Grade IVa is single organ dysfunction (including dialysis), Grade IVb is multi-organ dysfunction. Grade 5 is death of the patient.

Below is a list of the clinically important difference magnitudes for the different outcomes commonly used in BPH research.

Table 19. Overview of outcome measures from published or clinical expert opinion – minimally important change (Ray et al. (2015))

Outcome	Minimally important change
IPSS (Negative score is improvement)	Minimum = 3.0 Moderate = 5.1 Marked change = 8.8 (Barry et al. 1995)
IPSS QoL (Negative score is improvement)	Minimum = 1-3 (Clinical expert opinion)
IIEF (Positive score is improvement)	Minimum = 4 (Clinical expert opinion)
Qmax (ml/s) (Positive is improvement)	Minimum = 2ml/s (NICE CG97)
PVR (ml) (Negative is improvement)	Minimum = 50 ml (Clinical expert opinion)

Appendix 2. Search strategies and PRISMA flow numbers

Searches conducted 5/6th October 2015

Medline 1946 to Present with Daily Update
1. Prostatic Hyperplasia/ (18835)
2 benign prostatic hyperplasia.mp. (9788)
3 prostatic enlargement.mp. (564)
4 1 or 2 or 3 (21022)
5 Laser Therapy/ (34110)
6 greenlight.mp. (170)
7 pvp.mp. (4113)
8 photoselective vaporisation.mp. (26)
9 photoselective vaporization.mp. (207)
10 180-W xps.mp. (6)
11 4 and 5 (933)
12 6 or 7 or 8 or 9 or 10 (4260)
13 4 and 12 (270)
14. 11 or 13 (988)
15 limit 14 to "therapy (maximizes sensitivity)" (560)

Embase <1974 to 2015 October 06
prostate hypertrophy/ (30276)
2 benign prostatic enlargement.mp. (560)
3 benign prostatic hyperplasia.mp. (14776)
4 1 or 2 or 3 (32254)
5 greenlight.mp. (525)
6 pvp.mp. (7447)
7 photoselective vaporisation.mp. (97)
8 photoselective vaporization.mp. (497)
9 180-w xps.mp. (31)
10 5 or 6 or 7 or 8 or 9 (7790)
11 4 and 10 (593)
12 limit 11 to "therapy (maximizes sensitivity)" (273)

The above Medline and Embase searches were repeated on 13.11.2015 as the EAC became aware of further relevant citations. Eleven extra citations had been indexed in Medline and Embase since the original searches. Two of these were included (Jovanovic 2014 and Hueber 2015). Citations identified in the update were as follows:

- Medline 567 (original 560)
- Embase 277 (original 273)
- Additional citations 11
- Additional papers cited 3
- Total 844 (743 after removing duplicates).

Cochrane search

1 Greenlight:ti,ab,kw (Word variations have been searched)
All results 54
Cochrane Database of Systematic Reviews : Issue 11 of 12, November 2015 0
Database of Abstracts of Reviews of Effect : Issue 2 of 4, April 2015 3
Cochrane Central Register of Controlled Trials : Issue 10 of 12, October 2015 45
Health Technology Assessment Database : Issue 4 of 4, October 2015 4
NHS Economic Evaluation Database : Issue 2 of 4, April 2015 2

PRISMA flow numbers

Number of citations found in searches by EAC team = 887
Additional citations identified in updated search (13.11.2015) = 11
Additional references = 3
Additional references included = 2 (Hueber 2015, Jovanovic 2014)
Total number of citations = 898
Number of included studies in narrative review: 15
Number of full text papers excluded: 32
Number in meta-analysis = 0

Average risk patients:
RCTs of GreenLight 180W vs TURP = 2 (GOLIATH (3 articles), Jovanovic (1 article))
High risk patients:
Anticoagulants
180W GreenLight - Chung 2012,
120W GreenLight - Woo 2011, Woo 2008, Cakiroglu 2013, Chen 2013a, Chen 2013b, Sohn 2011, Tam 2012, Tao 2013
Larger prostates
180W GreenLight – RCT: Elshal 2015
180W GreenLight - Case series: Altay 2015, Hueber 2015, Nicholson 2015, West 2015
120W GreenLight RCT – Elmansy 2012
Urinary retention
Woo 2011, Woo 2008.

As some of the excluded studies were clinical studies of GreenLight, the reasons for exclusion of the principal studies are given below.

Table 20. Table of principal excluded GreenLight clinical studies

Reference	Study design and reason for exclusion
Elshal, A.M., et al., *Holmium:YAG transurethral incision versus laser photoselective vaporization for benign prostatic hyperplasia in a small prostate.* Journal of Urology, 2014. **191**(1): p. 148-54.	Study design: RCT Used GreenLight 80w and does not report a high risk group.

Elshal, A.M., H.M. Elmansy, and M.M. Elhilali, *Two laser ablation techniques for a prostate less than 60 mL: lessons learned 70 months after a randomized controlled trial.* Urology, 2013. **82**(2): p. 416-22. Elmansy, H.M., E. Elzayat, and M.M. Elhilali, *Holmium laser ablation versus photoselective vaporization of prostate less than 60 cc: long-term results of a randomized trial.* Journal of Urology, 2010. **184**(5): p. 2023-8. Elmansy, H. and M. Elhilali, *Holmium laser ablation (HOLAP) versus photoselective vaporization (PVP) of prostate < 60cc: Long term results of a randomized trial.* Journal of Urology, 2010. **1)**: p. e742. Elzayat, E.A., et al., *Holmium laser ablation of the prostate versus photoselective vaporization of prostate 60 cc or less: short-term results of a prospective randomized trial.* Journal of Urology, 2009. **182**(1): p. 133-8.	Other reports of this study also excluded.
Capitan, C., et al., *GreenLight HPS 120-W laser vaporization versus transurethral resection of the prostate for the treatment of lower urinary tract symptoms due to benign prostatic hyperplasia: a randomized clinical trial with 2-year follow-up.* European Urology, 2011. **60**(4): p. 734-9.	Study design: RCT Uses GreenLight 120-W and is not in a high-risk group. Although prostate size is considered the cut-off is >=50cm^3 not >=100ml. Previous catheterisation might indicate retention but in both cases numbers in subgroups are not given. No safety information by subgroup is provided.
Elkoushy, M.A., A.M. Elshal, and M.M. Elhilali, *Postoperative lower urinary tract storage symptoms: Does prostate enucleation differ from prostate vaporization for treatment of symptomatic benign prostatic hyperplasia?* Journal of Endourology, 2015. **29**(10): p. 1159-1165.	GreenLight 80-w, 120-w, 180-w results are combined in this prospectively collected database study and are not reported separately.
Elshal, A.M., et al., *Male sexual function outcome after three laser prostate surgical techniques: a single center perspective.* Urology, 2012. **80**(5): p. 1098-104. Elshal, A.M., H.M. Elmansy, and M.M. Elhilali, *Can we predict the outcome of 532 nm laser photoselective vaporization of the prostate? Time to event analysis.* Journal of Urology, 2012. **188**(5): p. 1746-1753. Elkoushy, M.A., A.M. Elshal, and M.M. Elhilali, *Postoperative lower urinary tract storage symptoms: Does prostate enucleation differ from prostate vaporization for treatment of symptomatic benign prostatic hyperplasia?* Journal of Endourology, 2015. **29**(10): p. 1159-1165. Elshal, A.M., H.M. Elmansy, and M.M. Elhilali, *Transurethral laser surgery for benign prostate hyperplasia in octogenarians: safety and outcomes.* Urology, 2013. **81**(3): p. 634-9.	Study design: prospective database The first two studies listed used GreenLight 80-w. In the other papers, Greenlight 80-w, 120-w, 180-w results are combined in this prospectively collected database study and are not reported separately.

Telli, O., et al., *A prospective, randomized comparative study of monopolar transurethral resection of the prostate versus photoselective vaporization of the prostate with GreenLight 120-W laser, in prostates less than 80 cc.* Therapeutic Advances in Urology, 2015. **7**(1): p. 3-8.	Study design: RCT GreenLight 120w not in a high risk population

Appendix 3. Comparison of 180-W vs 120-W GreenLight laser treatment for LUTS due to BPH.

GreenLight 180-W XPS has superseded GreenLight 120-W HPS, so the question arises of whether the outcomes associated with GreenLight 180-W XPS differ from those of GreenLight 120-W HPS. As the mechanism of action remains the same, outcomes which might be expected to associated with extra power, such as operating time, may be those most susceptible to change but all outcomes are of interest.

From the GreenLight searches conducted for the project, a sift was made to look for any studies comparing 180-W to 120-W GreenLight laser treatment for LUTS due to BPH. This was supplemented by searching within the recent systematic reviews of GreenLight laser treatment for relevant studies. There were 5 studies found. The characteristics of these studies are in Table 21, the baseline results in Table 22 and follow up results in Table 23.

Table 21. Characteristics of 180-W vs 120-W GreenLight laser treatment studies

	Country, study design	N 180-W	N 120-W	Follow up	Follow up outcomes given
Ben-Zvi 2013	Canada, prospective cohort	120 (64 on anti-coagulants)	80 (38 on anti-coagulants)	Baseline, 30 days, 3 month, 6 month	IPSS, QoL, QMax, PVR, PSA, complications
Campbell 2013	Australia, Prospective case series	50	50	Baseline, 3 months	IPSS, QoL, QMax, PVR, PSA, IIEF, complications-retention
Eken 2015	Turkey, Prospective cohort	73 (29 on anti-coagulants)	88 (23 on anti-coagulants)	Baseline, 1 month, 6 months	IPSS, QoL, QMax, PVR, average flow, complications
Hueber 2013	Multicentre (Canada, Australia, USA, UK). Retrospective case series	622 (359 for operating time, less for other measures)	1187 (658 for operating time, less for other measures)	Baseline only	None
Rieken 2013	Switzerland, retrospective case series	80	80	Baseline, 3 months	IPSS, QoL, QMax, PVR, PSA, complications

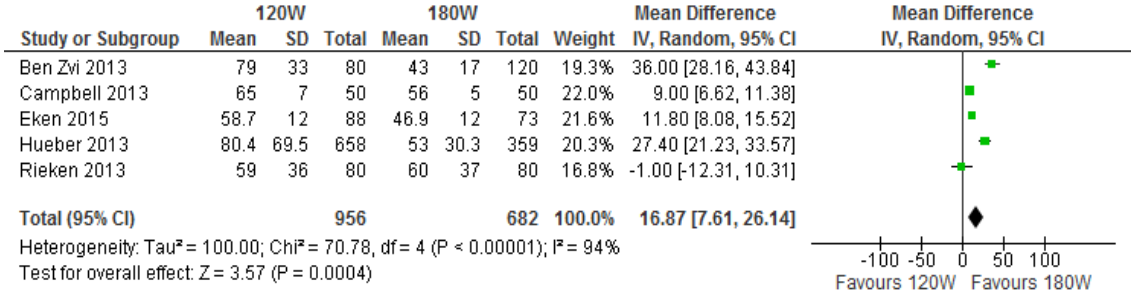
Table 22. Baseline results of 180-W vs 120-W GreenLight laser treatment studies

		Operating time (mins)	Capsular perforation	Mean hospital (days or hrs)	Mean fibre use
Ben-Zvi 2013	120-W	79 (24-223)	1 (1.2%)	1.5 (0-5)	1.5 (1-5)
	180-W	43 (15-118)	5 (4.1%)	0.3 (0-2)	1.0 (1-2)
Campbell 2013	120-W	65 (49.5-92)	0	19 (16-20.5)	ng
	180-W	56 (46-78.5)	1 (2%)	18 (16.3-20.8)	ng
Eken 2015	120-W	58.7 (28-98)	ng	ng	ng
	180-W	46.9 (25-95)	ng	ng	ng
Hueber 2013	120-W	80.4 (SD 69.5)	ng	ng	2.3 (SD 1.8)
	180-W	53.0 (SD 30.3)	ng	ng	1.1 (SD 0.3)
Rieken 2013	120-W	59 (SD 36)	5 (6%)	5.9 (SD 4.0)	1.2 (SD 0.5)
	180-W	60 (SD 37)	7 (9%)	4.3 (SD 0.8)	1.2 (SD 0.4)

Table 23. Follow up results of 180-W vs 120-W GreenLight laser treatment studies

		30-day readmissions	30-day complications – retention	30-day complications – incontinence	30-day complications – retreatment	Clavien Dindo grade 3 or above
Ben-Zvi 2013	120-W	5 (6%)	13 (16%)	3 (3%)	1 (1%)	0
	180-W	5 (4%)	8 (6%)	2 (2%)	0	0
Campbell 2013	120-W	ng	0	ng	ng	0
	180-W	ng	1 (2%)	ng	ng	4
Eken 2015	120-W	ng	3 (3.4%)	4 (4.5%)	2 (2.3%)	ng
	180-W	ng	3 (4.1%)	3 (4.1%)	1 (1.4%)	ng
Hueber 2013	120-W	ng	ng	ng	ng	ng
	180-W	ng	ng	ng	ng	ng
Rieken 2013	120-W	ng	7 (9%)	ng	ng	ng
	180-W	ng	5 (6%)	ng	ng	ng

Figure 5. Forest plot of operating time for the five 120-W vs 180-W studies



Appendix 4. Economic study quality assessment

Table 24. Quality assessment of health economic study

Study name	**Thomas et al 2015**	
Study design		
Study question	**Response (yes/no/not clear/N/A)**	**Comments**
1. Was the research question stated?	Yes	The objective of the study was included in the abstract section: "To reassess the costs and effects of PVP versus transurethral resection of the prostate (TURP) on the basis of most recent data". p.376
2. Was the economic importance of the research question stated?	Yes	Detailed Introduction section describing the importance of the economic evaluation comparing PVP to TURP in an UK context. p.376-7
3. Was/were the viewpoint(s) of the analysis clearly stated and justified?	Yes	Healthcare perspective. p.378
4. Was a rationale reported for the choice of the alternative programmes or interventions compared?	Yes	PVP vs TURP (current standard when medical therapy fails). p.376-7
5. Were the alternatives being compared clearly described?	Yes	Both interventions are described in the Introduction section. p.376-7
6. Was the form of economic evaluation stated?	Not clear	The authors suggest in the title that a cost-effectiveness analysis was done. What the authors present is a cost-utility analysis since efficacy is assessed as QALYs.
7. Was the choice of form of economic evaluation justified in relation to the questions addressed?	Not clear	A cost-utility analysis is appropriate to address the objective of the study, although the authors do not state that this was the form of economic evaluation chosen.
Data collection		
8. Was/were the source(s) of effectiveness estimates used stated?	Yes	Clearly stated in p.378 and Table 2.
9. Were details of the design and results of the effectiveness study given (if based on a single study)?	Yes	The authors use multiple comparisons, one of which is based on the GOLIATH trial. Design and effectiveness results of this trial are summarised in the Introduction section. p.377
10. Were details of the methods of synthesis or meta-analysis of estimates given (if based on an overview of a number of effectiveness studies)?	Yes	Three of the comparisons were based on meta-analyses and some of the differences and rationale for using different meta-analyses is provided. p.378
11. Were the primary	Yes	Quality adjusted life years (QALYs)

outcome measure(s) for the economic evaluation clearly stated?		
12. Were the methods used to value health states and other benefits stated?	Yes	QALYs were estimated by multiplying the duration in each health state with the corresponding utility value. p.378
13. Were the details of the subjects from whom valuations were obtained given?	No	Details could have been provided for the GOLIATH trial subjects.
14. Were productivity changes (if included) reported separately?	No	
15. Was the relevance of productivity changes to the study question discussed?	Yes	Patients treated as day-case may obtain benefits in terms of time to return to work or time to return to daily activities. p.385
16. Were quantities of resources reported separately from their unit cost?	Yes	Table 2
17. Were the methods for the estimation of quantities and unit costs described?	Yes	The authors referenced sources for unit costs and quantities of resource utilisation.
18. Were currency and price data recorded?	Yes	Procedure costs were based on reference cost, Personal Social Services Unit (PSSRU), and British National Formulary (BNF) estimates (in 2013 pounds).
19. Were details of price adjustments for inflation or currency conversion given?	No	Price adjustments for inflation should have been carried out as some of the costs of complications (e.g. monthly cost of incontinence and blood transfusion) are based on 2010 prices.
20. Were details of any model used given?	Yes	
21. Was there a justification for the choice of model used and the key parameters on which it was based?	Yes	The authors chose the same model used in the 2008 HTA. p.377
Analysis and interpretation of results		
22. Was the time horizon of cost and benefits stated?	Yes	The time horizon is lifelong. p.378
23. Was the discount rate stated?	Yes	3.5%. p.378
24. Was the choice of rate justified?	No	Although the choice of discount rate was not justified, 3.5% is reasonable rate to use.
25. Was an explanation given if cost or benefits were not discounted?	N/A	

26. Were the details of statistical test(s) and confidence intervals given for stochastic data?	Yes	Random-effects analysis. p.379
27. Was the approach to sensitivity analysis described?	Yes	Probabilistic sensitivity analysis. p.379
28. Was the choice of variables for sensitivity analysis justified?	Not clear	Distributions of costs and effects seem to have been used for PSA, but it is unclear if the 95% CI estimates for baseline risks and risk ratios were also used in the PSA.
29. Were the ranges over which the parameters were varied stated?	Yes	Table 2
30. Were relevant alternatives compared? (That is, were appropriate comparisons made when conducting the incremental analysis?)	Yes	Table 3
31. Was an incremental analysis reported?	No	The authors do not report an incremental analysis, just the probabilities of acceptable cost-effectiveness ratios in different scenarios. p.379, 381
32. Were major outcomes presented in a disaggregated as well as aggregated form?	No	Merely presented in a disaggregated form. Table 3
33. Was the answer to the study question given?	Yes	
34. Did conclusions follow from the data reported?	No	The conclusions are based on different aspects presented within the study but does not focus on what was the primary objective (i.e. cost-effectiveness of PVP when compared to TURP.
35. Were conclusions accompanied by the appropriate caveats?	No	The conclusion is somewhat misleading and does not take into account the uncertainty of the results (i.e. sensitivity analysis shows differences in probability of PVP being cost-effective when compared to TURP).
36. Were generalisability issues addressed?	Yes	The sensitivity analysis seems to be robust and addresses generalisability of the results
Reviewer's comments		The risk ratios used in the model based in the 2008 meta-analysis and presented in Table 1 for incontinence, blood transfusion, TUR syndrome and UTI do not match those presented in the HTA by Lourenco et al (2008). An error seems to have been made when Armstrong et al (2009) evaluated the cost-effectiveness of surgical treatments for men with benign prostatic enlargement and used the data from Lourenco et

		al (2008) for PVP. It seems that the authors used the PVP data presented in Armstrong et al (2009) for the model. The procedure cost for PVP is unclear as this does not include the cost of the machine (Table 2 in Thomas et al. 2015); only the cost per fibre that would be used with PVP was included. Previous economic evaluations of GreenLight 120-W (Benejam-Gual et al 2014; Whitty et al 2013) – although not included in this review - have estimated the costs of capital equipment and training costs for PVP but it is not apparent if such costs were included in the Thomas et al (2015) paper. Additionally, the number of fibres used for PVP per patient may vary, having been estimated at a mean (SD) of 1.38 (0.61) fibres/patient (Whitty et al 2013). The difference in number of fibres needed per patient does not seem to have been taken into account in the Thomas et al (2015) model. The probability of requiring reoperation after PVP as compared with TURP used in the Whitty et al (2013) model was based on a meta-analysis by Thangasamy et al (2012) which has also been used in the Thomas et al (2015) study. The risk ratios (95% CI) presented in Thangasamy et al (2012) for reoperation were 1.87 (0.65–5.39), but are reported in Thomas et al (2015) as 1.62 (0.56-372). The authors suggest that more than 70% of the patients with PVP in the UK require less than 24 hours to achieve stable health and therefore could be treated as day cases. However, the median length of hospital stay for PVP in the GOLIATH trial was 49.3 hours (Bachmann et al 2014) and the reasons for the UK patients requiring less time is unclear. Judging by Figure 2 in Thomas et al (2015) there were more patients as day case with TURP than with PVP, therefore invalidating the author's assumptions at least for the overall patient population. Note, however, that Figure 2 is based on the data from all 9 countries where practice variation may be substantial.
Adapted from Drummond MF, Jefferson TO (1996) Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. British Medical Journal 313 (7052): 275–83. Cited in Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

Table 25: Quality assessment of health economic study

Study name	**Benejam-Gual et al 2014**	
Study design		
Study question	**Response (yes/no/not clear/N/A)**	**Comments**
1. Was the research question stated?	Yes	The objective of the study was included in the abstract section and introduction: "To analyse the costs associated with two surgical procedures for lower urinary tract symptoms secondary to benign prostatic hyperplasia: GreenLight XPS 180-W versus the gold standard transurethral resection of the prostate". p.373
2. Was the economic importance of the research question stated?	Yes	Authors state that "new technologies should be accompanied by the corresponding economic assessment demonstrating its efficiency". p.374
3. Was/were the viewpoint(s) of the analysis clearly stated and justified?	Yes	Spanish National Health System perspective. p.374
4. Was a rationale reported for the choice of the alternative programmes or interventions compared?	Yes	GL XPS 180-W vs TURP (endoscopic surgical technique of reference in the treatment of lower urinary tract symptomatology secondary to benign prostatic hyperplasia). p.374
5. Were the alternatives being compared clearly described?	Yes	Both interventions briefly described in the Introduction section. p.374
6. Was the form of economic evaluation stated?	Not clear	The authors describe the study as a retrospective study of costs. Although effectiveness data was collected (healing at 3 months) the authors did not produce a measure of cost-effectiveness. Therefore, this evaluation can be considered as a cost analysis. Cost data was collected retrospectively in a multicentre setting. P.374-5
7. Was the choice of form of economic evaluation justified in relation to the questions addressed?	Yes	The form of economic evaluation is justified because the authors only intended to analyse the costs associated with the interventions being evaluated.
Data collection		
8. Was/were the source(s) of effectiveness estimates used stated?	Yes	Effectiveness was assessed from the clinical histories of sequential patients operated between July 2012 and October 2012. Effectiveness was considered as healing at 3 months. p.374-5.

9. Were details of the design and results of the effectiveness study given (if based on a single study)?	Yes	p.374-5. The exclusion criteria however had potential to obtain biased results, which was not discussed at all in the article.
10. Were details of the methods of synthesis or meta-analysis of estimates given (if based on an overview of a number of effectiveness studies)?	N/A	
11. Were the primary outcome measure(s) for the economic evaluation clearly stated?	N/A	This can be considered as N/A as the authors present a partial economic evaluation in the form of cost analysis.
12. Were the methods used to value health states and other benefits stated?	N/A	As above.
13. Were the details of the subjects from whom valuations were obtained given?	Yes	Table 1, p.375. Patients' age, prostatic volume, PSA, IPSS and Qmax were compared between GreenLight and TURP.
14. Were productivity changes (if included) reported separately?	No	Indirect costs, including productivity were not assessed.
15. Was the relevance of productivity changes to the study question discussed?	No	Although productivity was not assessed, it could have been discussed since if the hospital stay is shown to be reduced, it can lead to a reduction in days of work absence when compared to TURP.
16. Were quantities of resources reported separately from their unit cost?	No	Quantities of resources and unit costs were not reported, only average costs per patient reported. This compromises on the transparency of the study results.
17. Were the methods for the estimation of quantities and unit costs described?	Yes	The authors state that resource use was obtained from the clinical notes and unit costs were obtained from specialised literature, public and professional agencies. p.375. No details as to what exactly was involved (e.g. what quantity multiplied by what unit cost) and whether any assumptions were needed to be made to arrive at the final costs were not reported.
18. Were currency and price data recorded?	Yes	2013 euros. p.375
19. Were details of price adjustments for inflation or currency conversion given?	Yes	Costs were adjusted according to the General Index of Consumer Prices. Currency conversion does not seem to have been necessary as the unit costs were obtained from Spanish sources. p.375
20. Were details of any model used	No	No model was used in this study. The

given?		reported 'mathematical model' is actually a simple arithmetic formula showing the sum of quantities of resource use times respective prices.
21. Was there a justification for the choice of model used and the key parameters on which it was based?	N/A	
Analysis and interpretation of results		
22. Was the time horizon of cost and benefits stated?	Yes	3 months. p.374
23. Was the discount rate stated?	N/A	
24. Was the choice of rate justified?	N/A	
25. Was an explanation given if cost or benefits were not discounted?	N/A	
26. Were the details of statistical test(s) and confidence intervals given for stochastic data?	Yes	Average costs per patient and 95% confidence intervals were provided for surgical and post-surgical phases but not for total costs. Tables 2-4
27. Was the approach to sensitivity analysis described?	Yes	Univariate sensitivity analysis of hospital stay and prostate size.
28. Was the choice of variables for sensitivity analysis justified?	Yes	Hospital stay and prostate size were considered by the authors as the most relevant variables. p.375
29. Were the ranges over which the parameters were varied stated?	Yes	Provided for length of hospital stay. p.376
30. Were relevant alternatives compared? (That is, were appropriate comparisons made when conducting the incremental analysis?)	N/A	Partial economic evaluation in the form of cost analysis.
31. Was an incremental analysis reported?	N/A	Partial economic evaluation in the form of cost analysis.
32. Were major outcomes presented in a disaggregated as well as aggregated form?	N/A	Partial economic evaluation in the form of cost analysis.
33. Was the answer to the study question given?	Yes	GL XPS 180-W is associated with a reduction in costs due to a shorter duration of hospital stay. p.376
34. Did conclusions follow from the data reported?	Yes	
35. Were conclusions accompanied by the appropriate caveats?	Yes	The authors acknowledge some limitations such as the small sample size and variability in medical practice across hospitals. p.376
36. Were generalisability issues addressed?	Yes	This was attempted by the authors by retrieving data from four different hospitals. p.376
Reviewer's comments	The authors concluded that the reduction in costs by	

	using GL XPS 180-W is due to a shorter duration of hospital stay. The results obtained seem to have been influenced by two of the four hospitals in which the length of hospital stay was one day or less for all patients treated with GL XPS 180-W. The results reported for the sensitivity analysis are not clear. The authors report that “the cost reduction can reach up to 698€ per patient in the first 3 months” but then state that “final outcomes are strongly influenced by variations in clinical practice”. The average length of stay of 1.31 days is substantially shorter than that observed in the GOLIATH trial (Bachmann et al 2014). The authors report a mean of 1.03 fibres used per patient which is lower than the 1.38 fibres/patient observed by Whitty et al (2013). The confidence interval at 95% for the costs of fibres is not provided and it is not clear if there was variation in number of fibres used in the four different hospitals. It is not clear how the authors estimated the costs of capital equipment for GL XPS 180-W, reported as 225€. There is no indication of which complications were associated with each intervention and the number of complications. Contrarily to what seems to have been observed in this study, the rates of adverse events observed in the GOLIATH trial were similar. As the details of the main assumptions including parameter values used in estimates are not described clearly in the paper, it is difficult to assess the validity of the results. In addition, the exclusion criteria coupled with forced statistical methods (trimmed averages) yielded very small standard errors around the costs. This appears to be far from real practice where one would expect some patients to have longer lengths of stays (they are not “extreme values” that could just be “removed”, p. 375).
Adapted from Drummond MF, Jefferson TO (1996) Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. British Medical Journal 313 (7052): 275–83. Cited in Centre for Reviews and Dissemination (2008) Systematic reviews. CRD’s guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination	

Document cover sheet

Assessment report: GID-MT564 GreenLight XPS for treating benign prostatic hyperplasia Guidance Update

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EAC sign-off: Andrew Sims

Version number	Brief description of changes	Author/reviewer (*e.g.* J Smith)	Date (DD/MM/YY)	Date sent to NICE (if applicable)
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0.02	Separate version adding content to study characteristics, outcomes, critical appraisal	K Keltie	02/12/2021	
0.03	Merged versions of report	K Keltie	13/12/2021	
0.04	Prioritisation of evidence	K Keltie	15/12/2021	
0.05	Outcomes QA	R Parker	16/12/2021	
0.06	Adding conclusions, Adding critical appraisal checklists	R Parker, K Keltie	20/12/2021	
0.07	Adding critical appraisal summary	K Keltie	21/12/2021	
0.08	Versions of report merged including economics	R Parker	21/12/2021	
0.09	Review, addition of economic model review and updated costs	AJ Sims, R O'Leary	22/12/2021	

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NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technologies guidance

GID-MT564 GreenLight XPS for treating benign prostatic hyperplasia (Guidance Update)

Assessment report update

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Number of attached appendices: 5

Purpose of the assessment report update

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

Declared interests of the authors

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

None.

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Responsibility for report

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

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Abbreviations

Term	Definition
5ARI	5-alpha reductase inhibitor
AAT	Antithrombotic therapy
ARU	Assessment report update
ASA	American Society Anethesiology
AUA	American Urological Association
BCI	Bladder contractility index
BMI	Body mass index
BOO	Bladder outflow obstruction
BPH	Benign prostatic hyperplasia
BPO	Benign prostatic obstruction
CDC	Centers for disease control and prevention
CI	Confidence interval
CIC	Clean intermittent catheterisation
CRD	Centre for reviews and dissemination
CUA	Canadian Urological Association
DHSC	Department of Health and Social Care
DOAC	Direct oral anticoagulant
DSA	Deteministic sensitivity analysis
DUA	Detrusor underactivity
DVT	Deep vein thrombosis
EAC	External Assessment Centre
EAU	European Association of Urology
ED	Erectile dysfunction
EjD-MSHQ	Ejaculatory domain of male sexual health questionnaire
GreenLEP	GreenLight laser enucleation of the prostate
HoLEP	Holmium laser enucleation of the prostate
HRG	Healthcare Resource Group
IFU	Instructions for use
IIEF	International index of erectile function
IPSS	International Prostate Symptoms Score
IQR	Interquartile range
ISI	Incontinence severity index
LoS	Length of stay
LUTS	Lower urinary tract symptom
MAUDE	Manufacturer and User Facility Device Experience
MHRA	Medicines and Healthcare products Regulatory Agency
MSHQ	Male sexual health questionnaire
MTEP	Medical Technologies Evaluation Programme
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NICE CG	NICE clinical guideline
NICE MTG	NICE medical technology guidance
NICE QS	NICE quality standard
NOAC	New oral anticoagulant
NR	Not reported

Term	Definition
OP	Open prostatectomy
PAE	Prostate artery embolisation
PEBE	Photoselective en-bloc enucleation
PGI-I	Patient global impression of improvement
PRESS	Peer Review of Electronic Search Strategies
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSA	Prostate specific antigen
PVP	Photoselective vaporisation of prostate
PVR	Post-void residual volume
Qmax	Maximum flow rate
QoL	Quality of life
QUORUM	Quality of Reporting of Meta-analyses
RCT	Randomised controlled trial
SD	Standard deviation
SHIM	Sexual health inventory for men
ThuLEP	Thulium laser enucleation of the prostate
ThuVEP	Thulium vapoenucleation of the prostate
TRUS	Transrectal ultrasound
TUIP	Transurethral incision of the prostate
TUR	Transurethral resection syndrome
TURP	Transurethral resection of the prostate
TUVP	Transurethral vaporisation of the prostate
UDS	Urodynamic study
UTI	Urinary tract infection
VAS	Visual analogue scale

Executive summary

In this Assessment Report Update (ARU), “Company” refers to Boston Scientific. “EAC” refers to the Newcastle External Assessment Centre, the authors of this ARU. “Clinical experts” refers to individuals, approved by NICE, who advised the EAC in the preparation of this report.

New clinical evidence (total of 65 studies) was submitted by the Company for the purpose of this ARU. Following an updated search by the EAC, a total of 58 new studies (including 25 identified by the Company) were considered relevant to the decision problem. The majority (50 of 58) included high-risk patients, however only 8 reported outcomes exclusively in high-risk patients (only 2 were comparative). A total of the 37 studies most relevant studies were appraised in this report comprising 1 RCT, 3 propensity matched cohorts, 7 non-randomised, non-propensity-matched comparative studies, and 26 cohort studies stratifying patients by risk groups (N=8), procedure setting (N=1) or those which reported on rare adverse events (N=17). The quality of the included studies was low to good with only one study conducted in the UK. The remaining 21 single-arm studies, considered in scope, were not summarised or critically appraised by the EAC due to the volume of evidence, and because these studies did not report on rare adverse events or day-case procedures.

GreenLight is associated with shorter duration of catheterisation and duration of hospital stay when compared with TURP. Quality of life measures were generally poorly reported; one propensity matched cohort study reported significantly higher ejaculatory function at 12 months with GreenLight than TURP. The GOLIATH trial, which was considered within the original Assessment Report, remains the only randomised evidence comparing GreenLight against TURP (mono- and bi-polar combined). No randomised evidence comparing GreenLight 180 W PVP to HoLEP has been identified. The identified RCT compared surgical techniques (ejaculatory hood sparing PVP versus standard PVP) and was set in Egypt. Results from the clinical evidence suggest that GreenLight 180 W XPS PVP can provide symptomatic relief of LUTS in patients with BPH including in patients considered of high-

risk (prostate volume greater than 100 ml, patients with preoperative urine retention, patients at risk of bleeding), with low occurrence of device-related adverse events. Twelve studies reported on the proportion of patients requiring blood transfusion; between 0% and 2.2% intraoperatively, and between 0.6% and 0.8% within 30 days. Seventeen studies recorded the proportion of patients experiencing capsular perforation; no events occurred in six studies, and range between 0.1 and 5.6% in the remaining studies. Transurethral resection syndrome was only identified in one patient across all included studies.

Six published economic studies were identified, two of which demonstrated GreenLight to be cost-saving when compared with TURP, one showed GreenLight to be more costly but more cost-effective than TURP, and one cost-saving when compared with HoLEP or ThuLEP (interventions were not reported exclusively). There is not enough robust new evidence to model high-risk groups separately as different scenarios. A decision tree model including a general population with six month time horizon showed GreenLight to be cost-saving when compared with TURP (£69 per patient), and cost-incurring when compared with HoLEP (£114 per patient) when accounting for increased use of HoLEP per year. Cost savings with GreenLight (compared with both TURP and HoLEP) were achieved if the proportion of patients receiving GreenLight as a day-case procedure increased from 36% (in the original Assessment Report) to 68% (in this Assessment Report update) in line with a single UK published study. Univariate threshold analysis indicated that day-case procedures would have to be conducted in 43.6% of TURP, and 56% of HoLEP for GreenLight to be considered cost-incurring. A Markov model approach that modelled longer-term consequences over a 5 year time horizon showed GreenLight to be cost-saving by £305 and £270 when compared with TURP and HoLEP respectively. Probabilistic sensitivity analysis was limited due to lack of data, but found GreenLight to be cost-saving in 83% and 75% of simulations when compared to TURP and HoLEP respectively, when using the Company's estimates of uncertainty. However, with lack of robust comparative data on key parameters (such as length of stay and procedural duration) and variation in both clinical practice and

variation in patient risk profile, there remains some uncertainty regarding the magnitude of cost-savings.

1 Decision problem

The Company has not proposed any variation to the decision problem specified in the final scope (NICE MT564 Final Scope, 2021), Table 1.

Table 1: Scope of the decision problem

Decision problem	Scope	Proposed variation in Company submission
Population	People with urinary outflow obstruction secondary to benign prostatic hyperplasia in whom surgical intervention is indicated, especially those with prostates that are larger than ≥30ml.	No variation
Intervention	Greenlight XPS Photoselective Vaporisation of the Prostate (PVP).	No variation
Comparator(s)	• Monopolar and bipolar transurethral resection of the prostate (TURP) • Holmium laser enucleation of the prostate (HoLEP)	No variation
Outcomes	The outcome measures to consider to be included: **Patient outcomes** • symptoms of BPH (International Prostate Symptom Score [IPSS] • change in prostate volume • maximum flow rate (Qmax) • post void residual volume (PVR) • duration of catheterisation • rate of dysuria (pain) • quality of life measures, *e.g.*, International Prostate Symptom Score Quality of Life (IPSS-QOL) • preservation of sexual function **System outcomes** • length of hospital stay • frequency of completion as a day-case • rate of re-admission • procedural blood loss and blood transfusion requirement **Adverse effects** • rate of transurethral resection syndrome (TUR) • rate of capsular perforation • device related adverse events	No variation
Cost analysis	Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be long enough to reflect differences in costs and consequences between the technologies being compared.	No variation

	Comparators: monopolar TURP, bipolar TURP and holmium laser enucleation of the prostate (HoLEP). Monopolar, and bipolar TURP should be included as in-patient procedures in the cost model to reflect the setting they are routinely used in the NHS. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers and combinations of devices are needed.	
Subgroups to be considered	• **High risk patients** should be considered as a subgroup due to the different resource consequences for this population. This group may include: • people with pacemakers or defibrillators and those at risk of bleeding sequelae (including people on anticoagulation therapy, with a history of bleeding disorders, an implanted prosthetic heart valve, implanted coronary stents, patients on aspirin therapy for prior coronary events, patients with prior deep vein thrombosis [DVT] or a high risk of DVT, stroke survivors, haemophiliacs, and patients who do not wish to have blood transfusions). • people with a prostate size greater than 100ml • people with urinary retention • **Settings** of the procedure should be considered as separate groups given the cost implications from this. The procedure is expected to be carried out as a day-case, but a small proportion of individuals may be admitted as inpatients.	No variation
Special considerations, including those related to equality	The condition of BPH is most common in men over the age of 50, so the GreenLight XPS laser system is primarily for use in this population. This is a function of the clinical condition for which the technology is indicated and is not likely to be considered an equalities issue. LUTS secondary to BPH are more prevalent in black men than men of white or Asian origin. This is also a function of the clinical condition, not of the technology itself. Laser vaporisation technology such as GreenLight has the potential to reduce the risk of bleeding compared with other surgical options and so may improve access to medical treatment for BPH in these previously excluded groups. These may include people on anticoagulant therapies, those with bleeding disorders and those whose beliefs prevent them from receiving blood transfusions, many of whom may be covered under the 2010 Equality Act. This technology may be appropriate for individuals who do not identify as male but have a prostate and may have BPH that requires treatment. Gender is a protected characteristic under the 2010 Equality Act.	Company quantified higher BMI as 40 or higher. No variation.

	Greenlight is contraindicated for people with prostate cancer. Cancer is recognised as a disability. Disability is a protected characteristic under the 2010 Equality Act.	
Abbreviations: BMI, body mass index; BPH, benign prostate hyperplasia; DVT, deep vein thrombosis; HoLEP, Holmium laser enucleation of the prostate; IPSS-QoL, International Prostate Symptom Score Quality of Life; LUTS, lower urinary tract symptoms; PVP, photoselective vaporisation of the prostate; PVR, post void residual volume; TUR, transurethral resection syndrome; TURP, transurethral resection of the prostate		

The EAC has made the following clarifications on other aspects of the scope.

- Population: all patients for which GreenLight XPS 180 W PVP is indicated for relief of symptoms relating to BPH.

- Intervention: The Company introduced the GreenLight 80 W system in 2005. This was followed by the 120 W HPS model and, most recently the 180 W XPS model that was the subject of the MTG29 GreenLight XPS Guidance. Only the use of GreenLight XPS 180 W device is considered in scope for this Guidance Update. Standard PVP, anatomical PVP and vaporesection or vapoincision are procedures available using GreenLight XPS and considered within scope in this Assessment Report Update (ARU), including ejaculation sparing surgical techniques.

    - *Standard photoselective vaporisation (PVP) technique*

      During standard PVP the GreenLight MoXy Laser Fiber is passed through a cystoscope (a tube with an imaging system), which is inserted into the urethra. A cavity is created where the prostate gland can be vaporised centrifugally from the prostatic urethra towards the prostatic capsule (Ghahhari *et al.* 2021; Campobasso *et al.* 2020; EAC Correspondence Log, 2022).

    - *Anatomical vaporisation technique*

      During anatomical PVP once the capsule at the apex of the prostate is identified, a bilateral incision is created lateral to the verumontanum and the tip of the resectoscope is used to find

the anatomical plane between the prostatic capsule and the adenoma. Vaporisation of the tissue follows the plane toward the bladder neck (Ghahhari *et al.* 2021; Campobasso *et al.* 2020).

- *Vaporincision or vaporesection*
  Vapor-incision technique, also referred to as vaporesection, uses side-fire vaporisation along the capsule following ademona incisions with liberated tissue fragments retrieved from the bladder with grasping forceps or transurethral loops (Azizi *et al.* 2017; EAC Correspondence Log, 2022). There was variation amongst clinical experts; some described this technique as similar to PVP, whilst others described as similar to HoLEP or TURP. Whilst included in this assessment report update as a comparator for completeness, four of the clinical experts advised that technique is not commonly used in the UK (EAC Correspondence Log, 2022).
- *Ejaculation sparing technique*
  Ejaculation sparing, also referred to as antegrade ejaculation preservation, uses the anatomic PVP technique with the maintenance of a thin line of tissue around the verumontanum that prevents retropulsion of the dissected side lobe into the bladder and to direct ejaculate in the correct direction (Contreras *et al.* 2021; EAC Correspondence Log, 2022).

- Some hybrid procedures have been reported within the literature including GreenLEP, enucleation and photosensitive en-bloc enucleation and these have not been considered within this update in line with the Company Submission and advice from Clinical experts (EAC Correspondence Log, 2022).

- Subgroups: one Clinical expert stated that patients with urine retention would not be clinically considered as having higher risk of complications (EAC Correspondence Log, 2022). Another Clinical

expert suggested that nearly 50% of patients having surgery for BPH have urinary retention, and according to the BAUS Bladder Outflow Obstruction audit, 2019 43% of surgery for BOO was completed for patients with urinary retention (EAC Correspondence Log, 2022).

2 Overview of the technology

The GreenLight XPS system (Boston Scientific) is intended for laser vaporisation of the prostate as a surgical intervention in the treatment of benign prostatic hyperplasia (BPH) and associated symptoms. The GreenLight XPS system comprises of an electronic console with screen, laser and a liquid cooled laser fibre system. The GreenLight XPS procedure reduces and removes enlarged prostatic tissue using photoselective vaporisation of prostatic tissue (PVP). The laser operates in the green range of the visible spectrum (532 nm) and is absorbed by oxyhaemoglobin (in blood and tissue) resulting in the vaporisation of the tissue, leaving no remaining fragments. PVP is delivered via a laser fibre that is passed through a cystoscope with a trans-urethral camera system. GreenLight XPS uses a proprietary laser delivery system which is an optical fibre, actively cooled using a flow of saline to minimise degradation and improve its durability intended for use with 22-26 Fr endoscopes or cystoscopes (the “MoXy” accessory). GreenLight XPS has a ‘coagulation’ mode, which uses a pulsating laser light to seal (cauterise) any bleeding resulting from PVP. The GreenLight XPS uses a laser that can be adjusted to a maximum power of 180 W in 5 W increments. Greenlight XPS PVP is generally performed under a general anaesthetic, can also be performed under spinal anaesthetic, and may be done as either a day-case or an inpatient procedure.

The GreenLight XPS console is a class IIb device and the MoXy disposable laser fibre accessory is a class IIa device, with valid certification provided by a Notified Body until 2024. The first CE marked version of GreenLight was available in 2005 with earlier versions of the technology (80 W, followed by 120 W HPS in 2007). The Company has confirmed that there have been no

changes to the technology since MTG29. No new indications or applications not covered by the original guidance have been declared by the Company or identified by the EAC in view of this ARU.

3 Clinical context

GreenLight XPS is intended for use for the treatment of BPH, or enlarged prostate, and its associated symptoms, including lower urinary tract symptoms (LUTS) and bladder outflow obstruction (BOO), through the reduction and removal of excess prostate tissue. Current surgical treatment options for BPH when conservative management options have been unsuccessful or are not appropriate are found within the NICE Guideline on LUTS (CG97, 2015) and include:

- Monopolar or bipolar transurethral resection of the prostate (TURP),
- Transurethral vaporisation of the prostate (TUVP),
- Holmium laser enucleation of the prostate (HoLEP),
- Transurethral incision of the prostate (TUIP) (for prostates estimated as smaller than 30 ml),
- Open prostatectomy (OP) (for prostates estimated as larger than 80 ml).

The initial MTG29 GreenLight XPS Guidance supported the use of GreenLight XPS for treating BPH in patients not considered of high-risk. The Company have submitted new evidence to support the routine adoption of GreenLight XPS in high-risk patients, which is those who:

- have increased risk of bleeding, or
- have prostates larger than 100 ml, or
- have urinary retention.

The European Association of Urology (EAU) Guideline for the Management of Non-neurogenic Male LUTS 2022 reports that GreenLight 180 W PVP "seems to be safe for the treatment of patients receiving antiplatelet or anticoagulant therapy"; however, the level of available evidence was reported as "low".

The Canadian Urological Association (CUA) Guideline on Male Lower Urinary Tract Symptoms/Benign Prostatic Hyperplasia (MLUTS/BPH) 2018 conditionally recommends GreenLight PVP as an alternative surgical approach in men on anticoagulation or with a high cardiovascular risk based on moderate quality evidence.

The American Urological Association (AUA) Guideline for the Management of Benign Prostatic Hyperplasia/Lower Urinary Tract Symptoms 2021 recommends, based on expert opinion, that PVP is considered as a treatment option in patients who are at higher risk of bleeding. The AUA guideline discussion notes that surgeons should be aware that longer catheterisation and irrigation are associated with an increased rate of complications and longer hospitalisation.

Special considerations, including issues related to equality

From the Instructions for Use (IFU), GreenLight XPS is contraindicated in patients: whose general medical condition contraindicates surgical intervention, when appropriate anaesthesia is contraindicated by patient history, where tissue (especially tumours) is calcified, for haemostasis of vessels over approximately two millimeters in diameter, where laser therapy is not considered the treatment of choice, uncontrolled bleeding disorders and coagulopathy, prostate cancer, acute urinary tract infection, or severe urethral stricture.

BPH is common in men over 50 years and its incidence increases with age; BPH incidence estimated to increase from 50% in men between the ages of 50 to 60 years to 90% for men over the age of 80 years (Urology Foundation). This is a function of the clinical condition for which the technology is indicated and is not likely to be considered an equalities issue.

GreenLight XPS may be appropriate for individuals who do not identify as male but have a prostate and may have BPH that requires treatment. Gender is a protected characteristic under the 2010 Equality Act. The technology is not contraindicated in these patients; alterations to surgical technique to access the prostate tissue may need to be considered in line with any alternative surgical intervention in such cases. One Clinical expert has experience treating two transgender patients with GreenLight XPS with no differences in procedure outcomes reported. Another Clinical expert identified that transgender patients may have a shorter urethra and so power settings may need to be carefully considered (EAC Correspondence Log, 2022).

GreenLight XPS Laser System IFU state it is contraindicated for some people including those with prostate cancer and uncontrolled bleeding disorders. Cancer is recognised as a disability and disability is a protected characteristic under the 2010 Equality Act.

LUTS secondary to BPH are more prevalent in black men than men of white or Asian origin, and is also considered a function of the clinical condition rather than the technology.

Laser vaporisation technology, such as GreenLight XPS, has the potential to reduce the risk of bleeding compared with other surgical options. This may improve access to medical treatment or surgical intervention for BPH in these previously excluded groups including those on anticoagulant therapies or those whose beliefs prevent them from receiving blood transfusions, many of whom may be covered under the 2010 Equality Act.

There is a well-established link between sexual dysfunction and LUTS secondary to BPH in addition to the potentially negative impact from surgical or medical intervention on sexual function (Abolazm *et al.* 2020; Destefanis *et al.* 2021; DeLay *et al.* 2016). This is considered a function of both the clinical condition as well as the intervention and so sexual outcomes should be considered within the guidance.

4 Clinical evidence selection

4.1 *Evidence search strategy and study selection*

As requested by NICE, this search was designed to identify any new potentially relevant evidence for this guideline update (GID-MT564) that had been published since the search conducted in 2015 for the original version of the guideline (MTG29).

A literature search was developed by the EAC, using the following concepts: benign prostatic hyperplasia (BPH) AND (GreenLight XPS laser photovaporisation OR Boston Scientific). The searches were based on information from a number of sources including the NICE final scope (NICE MT564 Final Scope, 2021) and additional information shared by NICE at the project initiation meeting. At the start of this project only the original 2015 searches, undertaken by the Birmingham and Brunel NICE EAC for the original 2016 guideline, were available. These searches were critiqued using the Peer Review of Electronic Search Strategies (PRESS) tool (McGowan *et al.* 2016), Appendix A1. Based on the findings of this critique and information gained at the NICE project initiation meeting, the original 2015 search was adapted to cover alternative spellings, synonyms and to increase precision by use of proximity searching and removal of a very broad vocabulary term. The set of BPH terms developed was compared with those used in a number of previous NICE BPH-related guidelines MTG53 PLASMA (NICE, 2021) and MTG58 UroLift (NICE, 2021) as well as a recent Cochrane Urology BPH-related review (Franco *et al.* 2021). Any potentially relevant terms were tested to see if they added any additional relevant records to the search and were added if found useful.

Newcastle EAC received the Company search strategy (2021) after the initial search was developed. This tool was critiqued using the Peer Review of Electronic Search Strategies (PRESS) tool (McGowan *et al.* 2016), Appendix A1. The Company search strategy used redundant search concepts, did not translate the searches robustly into other databases and made inaccurate use of some controlled vocabulary terms. Further, the use of time limits (2020 to

2021) was not justified. Any potentially relevant terms were tested to see if they added any additional relevant records to the search and would have been added if found useful. At this stage, there were no additional useful terms to add.

The final search strategy was developed in Ovid MEDLINE and recall was tested using several preliminarily identified relevant papers. The use of some in-scope controlled vocabulary terms was tested for MEDLINE on MeSH and Embase on Emtree, however to keep to precision, those terms that did not add value to the search by identifying additional studies, were not used. This search strategy was checked by a second information specialist. The strategy was then translated into other relevant databases (Appendix A2). The searches were run on: MEDLINE, MEDLINE In-Process & In-Data-Review, Epub Ahead of Print and Daily and Embase (all via Ovid and all searched on 25 November 2021) the MEDLINE search was re-run on 15 December 2021 as a typographical error on the search had been identified; Cochrane Database of Systematic Reviews (CDSR) and CENTRAL (both on the Cochrane Library, via Wiley, and both searched on 29 November 2021); The International Network of Agencies for Health Technology Assessment database; ClinicalTrials.gov; World Health Organisation International Clinical Trials Registry Platform and IDEAS/RePEC database (all searched on 30 November 2021). The original Birmingham and Brunel NICE EAC search had included the DARE and NHS EED databases (on the Centre for Reviews and Dissemination (CRD) website, University of York, UK) these were not searched as part of this update since no further records have been added to these databases since they were last searched in 2015. The HTA database had also originally been searched on the CRD website in 2015 (it is still available via CRD although records have not been added since 2018), however its content has been transferred to the INAHTA database and is now regularly updated and so only the INAHTA database has been searched for this guideline update.

Searches were limited to English language articles using the limits available within Ovid. This means that there could be relevant non-English articles that

have been missed, including those not yet indexed as English language articles in the databases. A search filter was used in MEDLINE and Embase to remove animal only studies from the search results, this is because only human or human and animal studies are relevant. In Embase the conference abstract related 'publication type' (.pt.) was removed from results as for this guidance NICE did not require conference abstracts. As this is a search update, a number of date-related fields were searched to try to identify only records added to databases since the last search was run. The date-related set of terms were applied in the fully indexed MEDLINE database (and not in the other MEDLINE databases), and Embase. Year of publication limits were applied in CENTRAL, CDSR, and INAHTA. Date or year of publication limits were imposed to cut down on the sifting burden and to avoid duplication of effort with what had been screened for the earlier version of this guideline.

The records from each database searched were imported into one EndNote library (EndNote X.9) and de-duplicated firstly by using the functionality available within EndNote and secondly by manual checking. A total of 934 results were initially retrieved, of which 554 remained after deduplication.

The title and abstract of each were sifted according to the final scope (NICE GID-MT564 Final Scope, 2021) by a single reviewer. Full papers were retrieved and reviewed by a single reviewer. Included papers were reviewed by a second reviewer. The terminology relating to the intervention was found to be variable across the published literature. Studies describing PVP using 180 W laser were included, however studies describing different power setting, no power setting or no mention of GreenLight or Boston Scientific (manufacturer) were excluded. The EAC relaxed the comparator inclusion criteria (such as single-arm studies) due to those studies being relevant to some outcomes and having the potential to detect adverse events. The selection process is illustrated as a PRISMA diagram in Appendix A3.

4.2 *Included and excluded studies*

The Company identified a total of 65 studies they considered were relevant and within the scope of the decision problem. The EAC excluded 40 of these, Appendix A4.

A total of ten systematic reviews were also identified by the EAC; the primary evidence of each was reviewed, Appendix A5. Three additional systematic reviews were excluded as the primary evidence was published prior to the original Guidance Report (Albisinni *et al.* 2017; Li *et al.* 2016; Marra *et al.* 2016) and one further systematic review was excluded as GreenLight PVP procedure and 180 W power was not reported exclusively (Taratkin *et al.* 2021).

The EAC identified a total of 58 publications (including 25 identified by the Company), relevant to the decision problem reporting on outcomes defined in the final scope (NICE MT564 Final Scope, 2021), Table 2. The majority of studies (50 of 58, 86%) included high-risk patients, but only 8 studies reported outcomes exclusively. Note that, due to the large volume of evidence, the EAC focused on a total of 37 studies which included:

- 11 comparative studies, Table 3a,
- 8 cohort studies reporting exclusively in high-1risk group population or as a subgroup (using the definition of high-risk as outlined in the decision problem, NICE MT564 Final Scope, 2021), Table 3b,
- 1 cohort study which reported on day-case procedures, Table 3b.
- 17 single-arm studies reporting on rare adverse events outcomes only, Table 3c.

The EAC considered the remaining 21 single-arm studies in scope, however given the volume of identified evidence, and because these additional single-arm studies did not report on rare adverse outcomes or day-case procedures, they were therefore not summarised or critically appraised in the ARU.

Table 2: Identified studies and reported outcomes (N=58)

			Population: high-risk criteria			Efficacy outcomes								Safety outcomes						
Studies selected by the EAC as the evidence base:	Author (year)	Study design (n)	Prostate volume >100ml	Urinary retention	Risk of bleeding	IPSS	Change in prostate volume	Max flow rate (Qmax)	Post void residual volume (PVR)	Duration of catheterisation	Rate of dysuria (pain)	QoL	Sexual function	LoS	Day-case	Readmission	Blood loss	Transurethral resection syndrome	Capsular perforation	Adverse events
Comparative studies (N=11)	Abolazm *et al.* (2020)	RCT (n=49†)				✓		✓	✓	✓		✓	✓	✓		✓				✓
	Azizi *et al.* (2017)	Propensity matched cohort (n=444)	✓*	✓*	✓*	✓		✓	✓			✓				✓			✓	✓
	Cimino *et al.* (2017)	Propensity matched cohort (n=110)				✓		✓		✓			✓							✓
	Castellani *et al.* (2018)	Propensity matched cohort (n=90)			✓*	✓		✓		✓		✓		✓		✓	✓			✓
	Hibon *et al.* (2017)	Prospective non-randomised (n=106)	✓*	✓*	✓*	¶	¶	¶	¶	✓		¶		✓			✓			✓
	Mattevi *et al.* (2020)	Prospective non-randomised (n=100)			✓*	✓		✓		✓	✓			✓		✓	✓			✓
	Cindolo *et al.* (2017)	Retrospective non-randomised (n=813)	✓*	✓*	✓*	✓		✓		✓		✓		✓		✓	✓		✓	✓
	Reimann *et al.* (2019)	Retrospective non-randomised (n=254)		✓*	✓*					✓		¶		✓		✓	✓			✓
	Mathieu *et al.* (2017)	Retrospective non-randomised (n=237)	✓*	✓*	✓*									✓		✓				✓
	Gondran-Tellier *et al.* (2021)	Retrospective non-randomised (n=171)	✓*	✓	✓*					✓				✓		✓				✓
	Mesnard *et al.* (2021)	Retrospective non-randomised (n=13)			✓					✓				✓		✓	✓			✓
Cohort studies reporting by high-risk subgroup or setting exclusively (N=9)	Campobasso *et al.* (2020)	Retrospective cohort (n=1,031)	✓	✓*	✓*	✓		✓		✓		✓		✓		✓	✓		✓	✓
	Meskawi *et al.* (2017)	Retrospective cohort (n=438)	✓	✓*	✓*	✓		✓	✓	✓				✓			✓		✓	✓
	Meskawi *et al.* (2019)	Retrospective cohort (n=422)	✓*		✓	✓		✓	✓	✓				✓		✓	✓			✓
	Lee *et al.* (2016)	Retrospective cohort (n=384)	✓*		✓	✓		✓	✓	✓		✓		✓		✓	✓			✓
	Waters *et al.* (2021)	Retrospective cohort (n=374)	✓*	✓*	✓					✓				✓		✓	✓			✓
	Knapp *et al.* (2017)	Retrospective cohort (n=373)		✓*	✓					✓				✓			✓		✓	✓
	Goueli *et al.* (2017)	Retrospective cohort (n=332)	✓*	✓	✓*	✓		✓	✓	✓		✓		✓		✓	✓			✓
	Xu *et al.* (2021)	Retrospective cohort (n=312)				✓		✓	✓	✓		✓		✓	✓	✓	✓	✓	✓	✓
	Eken and Soyupak (2018)	Retrospective cohort (n=233)			✓	✓	✓	✓	✓	✓	✓					✓	✓			✓
Single-arm studies reporting on rare adverse events (N=17)	Law *et al.* (2021)	Retrospective cohort (n=3,627)	✓*		✓*	✓		✓	✓	✓	✓	✓		✓		✓	✓		✓	✓
	Gasmi *et al.* (2021)	Prospective cohort (n=1,491)		✓*	✓*									✓		✓			✓	✓
	Rajih *et al.* (2017)	Retrospective cohort (n=941)	✓*	✓*	✓*	✓		✓	✓	✓		✓		✓		✓	✓		✓	✓°
	Trujillo *et al.* (2021)	Retrospective cohort (n=587)	✓*	✓*	✓*	¶				✓		✓		✓		✓	✓			✓°
	Castellucci *et al.* (2020)	Retrospective cohort (n=487)				✓		✓		✓				✓		✓	✓		✓	✓
	Reimann *et al.* (2018)	Retrospective cohort (n=375)		✓*	✓*					✓	✓	✓		✓			✓	✓		✓
	Zhou *et al.* (2017)	Retrospective cohort (n=328)			✓*	✓		✓	✓	✓		✓		✓	✓	✓	✓		✓	✓
	Ghahhari *et al.* (2021)	Prospective cohort (n=193)		✓*	✓*	✓		✓		✓		✓		✓		✓	✓		✓	✓
	Liu *et al.* (2020)	Retrospective cohort (n=150)	✓*		✓*	✓	✓	✓	✓	✓	✓	✓		✓		✓	✓	✓	✓	✓
	Ghahhari *et al.* (2018)	Retrospective cohort (n=140ǂ)		✓*	✓*	✓		✓		✓				✓		✓	✓		✓	✓
	Tao *et al.* (2019)	Prospective cohort (n=102)	✓*	✓*	✓*	✓	✓	✓	✓	✓				✓		✓	✓	✓	✓	✓

			Population: high-risk criteria			Efficacy outcomes								Safety outcomes						
Studies selected by the EAC as the evidence base:	Author (year)	Study design (n)	Prostate volume >100ml	Urinary retention	Risk of bleeding	IPSS	Change in prostate volume	Max flow rate (Qmax)	Post void residual volume (PVR)	Duration of catheterisation	Rate of dysuria (pain)	QoL	Sexual function	LoS	Day-case	Readmission	Blood loss	Transurethral resection syndrome	Capsular perforation	Adverse events
	Aboutaleb *et al.* (2018)	Retrospective cohort (n=75ł)				✓		✓	✓	✓		✓		✓			✓		✓	✓
	Chen and Chiang (2016)	Retrospective cohort (n=65ł)				✓	✓	✓	✓	✓	✓	✓		✓		✓	✓	✓		✓
	Thomas *et al.* (2019)	Retrospective cohort (n=58)		✓*	✓*	✓		✓	✓			✓		✓					✓	✓
	Trail *et al.* (2021)	Retrospective cohort (n=538)		✓*						✓				✓	✓	✓				✓
	Berquet *et al.* (2015)	Prospective cohort (n=134)	✓*	✓*	✓*	✓		✓	✓	✓		✓			✓	✓	✓			✓
	Ferrari *et al.* (2021b)	Prospective cohort (n=10)	✓*																	✓°
Single-arm studies not reporting rare adverse events (N=21)	Huet *et al.* (2019)	Prospective cohort n=200ł)	✓*	✓*	✓*					✓			✓	✓		✓				✓
	Lopez *et al.* (2016)	Prospective cohort (n=82ł)			✓*	✓	✓	✓				✓		✓		✓				✓
	Akhtar and Raina (2018)	Prospective cohort (n=34)	✓*	✓*	✓*	✓				✓	✓			✓			✓			✓
	Reale *et al.* (2020)	Retrospective cohort (n=1,077)			✓*	✓		✓		✓	✓	✓		✓		✓	✓			✓
	Barco-Castillo *et al.* (2020)	Retrospective cohort (n=675)		✓*	✓*	✓				✓		✓		✓			✓			✓
	Bausch *et al.* (2020)	Retrospective cohort (n=665)		✓*																✓
	Campobasso *et al.* (2021)	Retrospective cohort (n=434)		✓*						✓										✓
	Pierce *et al.* (2021)	Retrospective cohort (n=424)	✓*		✓*	✓		✓	✓			✓		✓		✓	✓			✓
	Ajib *et al.* (2018)	Retrospective cohort (n=370)		✓*	✓*	✓		✓	✓	✓	✓	✓	✓	✓		✓				✓
	Bastard *et al.* (2017)	Retrospective cohort (n=366)		✓*	✓*	✓		✓		✓				✓						✓
	Moiroud *et al.* (2019)	Retrospective cohort (n=305)	✓*		✓*	✓		✓	✓	✓		✓		✓		✓				✓
	Castellan *et al.* (2019)	Retrospective cohort (n=291)		✓*	✓*	✓		✓				✓								✓
	Plata *et al.* (2021)	Retrospective cohort (n=271)		✓*	✓*	✓				✓		✓		✓	✓*					✓
	Hu *et al.* (2016)	Retrospective cohort (n=256)	✓*	✓*		✓		✓	✓	✓				✓						✓
	Destefanis *et al.* (2021)	Retrospective cohort (n=76ł)		✓*	✓*								✓				✓			✓
	Contreras *et al.* (2021)	Retrospective cohort (n=77)				✓		✓	✓				✓							
	Hermanns *et al.* (2019)	Retrospective cohort (n=47)		✓*	✓*					✓							✓			✓°
	Sun *et al.* (2018)	Retrospective cohort (n=44ł)	✓*	✓*	✓*	✓		✓	✓	✓		✓					✓			✓
	Valdivieso *et al.* (2018)	Retrospective cohort (n=33)	✓	✓*		✓		✓	✓					✓		✓				✓
	Marchioni *et al.* (2018)	Retrospective cohort (n=18)	✓*		✓*															✓
	Barco-Castillo *et al.* (2019)	Case report (n=1)								✓	✓					✓				✓

			Population: high-risk criteria			Efficacy outcomes								Safety outcomes						
Studies selected by the EAC as the evidence base:	Author (year)	Study design (n)	Prostate volume >100ml	Urinary retention	Risk of bleeding	IPSS	Change in prostate volume	Max flow rate (Qmax)	Post void residual volume (PVR)	Duration of catheterisation	Rate of dysuria (pain)	QoL	Sexual function	LoS	Day-case	Readmission	Blood loss	Transurethral resection syndrome	Capsular perforation	Adverse events

Abbreviation: IPSS, International Prostate Symptom Score; RCS, retrospective cohort study; RCT, randomised control trial; PCS, prospective cohort study; QoL, quality of life; LoS length of stay; RCCS, retrospective comparative cohort study; ROCS, retrospective observational cohort study;

†number randomised
*included but not exclusively
¶ reported but excluded by EAC due to error/unfair comparison
ǂ treated as single-arm (comparator out of scope)
°specifically device-related events

Table 3a: Studies selected by the EAC as the evidence base: comparative studies (comparing intervention or GreenLight surgical technique) (N=11)

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Abolazm *et al.* (2020) †Egypt	RCT (n=49 randomised) Intervention: Ejaculatory hood-sparing GreenLight XPS 180 W PVP (n=25) ☒☑ Comparator: Standard GreenLight XPS 180 W PVP (n=24) ☑	Patients with LUTS secondary to benign prostatic obstruction in whom medical treatment failed (3 months) between November 2015 and September 2017. Inclusion criteria: sexual activity (continuous relationship with same partner), IPSS≥15, BOOI≥20, prostate volume (TRUS) between 30 and 80ml. Exclusion criteria: preoperative sexual dysfunction, ejaculatory dysfunction, prostate cancer, neurological disorders, detrusor hypocontractility, catheter dependent, patients with bladder stones. ☑ Setting: single centre, single surgeon	Primary: preserved AE at 1 year, change in sexual function, ejaculatory function, IIEF-15 score. Secondary: degree of LUTS relief (IPSS), Qmax, PVR, PdetQmax, bladder outlet obstruction index, complications, retreatment. ☑	Comparison of surgical technique (standard photoselective vaporisation vs. ejaculatory hood sparing vaporisation).

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Azizi *et al.* (2017) Canada & USA	Propensity matched retrospective cohort, (n=444) Intervention: GreenLight XPS 180 W PVP (n=222) ☑ Comparator: GreenLight XPS 180 W vapour-resection/vaporincision technique (n=222) ☑ Propensity-score matching 1:1 without replacement: age, ASA score, current anticoagulation use, preoperative urinary retention and prostate volume measured by TRUS.	Patients with LUTS secondary to BPH, treated with laser prostatectomy between August 2021 and August 2014. Surgical indications based on AUA and CUA guidelines. Exclusion criteria: prior pelvic radiation, histological diagnosis of prostate cancer, neurogenic bladder, impaired detrusor contractility, neurologic disorder or artificial urinary sphincter. ☑ Setting: Multi-centre (N=5); 5 surgeons	Changes in IPSS, QoL, PVR, Qmax, PSA measured at 6 months, complications and adverse events. ☑	High-risk (includes patients on anticoagulation, patients with preoperative urinary retention and patients with prostate volume >100ml, but not exclusively).

Cimino *et al.* (2017) †Italy	Propensity matched cohort (n=110 included for analysis due use of propensity score matching based on prostate volume, peak flow, IPSS) Intervention: GreenLight XPS 180 W PVP (n=55) ☑ Comparator: TURP (n=55) ☑	Consecutive patients undergoing PVP or TURP for relief of LUTS between January 2014 and January 2016. Inclusion criteria: age >50y, IPSS score >12, Qmax <15ml/s for 125-ml voided volume, PVR <350ml, prostate volume <90cm^3 on ultrasound, sexually active within 6m before index procedure, any other response to EjD-MSHQ excluding "could not ejaculate", ISI score ≤4. Exclusion criteria: active UTI at time of procedure, bacterial prostatitis within 1yr of index procedure, cystolithiasis within 3m of index procedure, obstructive medial lobe as accessed via ultrasound and cystoscopy, current urinary retention, urethral conditions preventing insertion of rigid 20F cystoscope, previous TURP or laser procedure, pelvic surgery or radiation; PSA ≥10 ng/l, history of prostate or bladder cancer, neurogenic bladder disease, neurological disorders, severe cardiac comorbidities, anticoagulants within 3 days (excluding up to 100mg acetylsalicylic acid), unwilling to report sexual function, other medical condition or comorbidity contraindicative for TURP/PVP. ☑ Setting: multi-centre (N=2)	Primary: BPH6 endpoint which is a composite of 6 elements (adequate relief from LUTS, high-quality recover experience, maintenance of erectile function, maintenance of ejaculatory function, maintenance of continence, avoidance of high-grade complications). Secondary: IPSS, SHIM, Qmax.☑	Non-randomised comparison of TURP and GreenLight PVP (propensity matched).

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Castellani *et al.* (2018) Italy	Propensity matched (n=90) Intervention: GreenLight XPS 180 W (n=291) ☑ Comparator: ThuVEP (RevoLix Duo 90W) with morcellator (n=214) ☒☑	Consecutive patients undergoing surgery for BPH between 2014 and 2017, according to EAU guidelines. Exclusion criteria: neurological disease, history of prostate cancer or previous urethral stricture or prostate surgery, concomitant surgery (urethrotomy, cystolithotripsy, transurethral resection of incidental bladder tumour). Suspicious prostate cancer was ruled out preoperatively with prostate biopsy. ☑ Setting: multi-centre (N=3 for GreenLight, different single centre for ThuVEP); multiple surgeons (NR)	IPSS, Qmax, duration of catheterisation, QoL, LoS, readmission, blood loss, complications. ☑	High-risk (includes patients taking antiplatelet and anticoagulation, history of indwelling catheter but not exclusively). Comparator (ThuVEP) out of scope.
Hibon *et al.* (2017) France	Prospective non-randomised (n=106) Intervention: GreenLight XPS 180 W PVP (n=55), GreenLight XPS 180 W anatomical vaporization (n=51) ☒☑	Patients undergoing standard or anatomical PVP as treatment for large prostate enlargement (prostates >80cm^3) between 1st December 2012 and 1st December 2013. Exclusion criteria: non-sterile pre-surgical urine bacterial culture. ☑ Setting: multi-centre (N=2); 2 surgeons	LoS, catheterisation time, complications, change in IPSS, PSA, Qmax, PVR, prostate volume, and urinary QoL at 1, 3, 6 & 12 months. ☑	Comparison of surgical technique (GreenLight PVP versus anatomical vaporisation). High-risk (patients taking anticoagulation, prostate volume >100ml, with catheter in place, but not exclusively).

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Mattevi *et al.* (2020) Italy	Prospective non-randomised (n=100) Intervention: GreenLight XPS 180 W PVP (n=50) ☑, TURP (n=50) ☑	Consecutive patients undergoing surgical treatment of BPH between March 2015 and March 2016, captured in prospectively maintained database. No exclusion criteria listed. ☑ Setting: single centre; 2 urologists per arm	IPSS, Qmax, PVR, duration of catheterisation, LoS, complications, retreatment and re-catheterisation rates, transfusion rates, dysuria.☑	High-risk (includes patients taking anticoagulation/antiplatelets but not exclusively)
Cindolo *et al.* (2017) Italy	Retrospective non-randomised (n=813) Intervention: GreenLight XPS 180 W, either standard PVP (n=403) or anatomical PVP (n=410); via surgeon preference. ☑	Patients undergoing standard and anatomical PVP between 2011 and 2016. Exclusion criteria: history of prostate cancer, neurological disease, contemporary urethrotomy, cystolithotripsy, incidental bladder tumours. ☑ Setting: multi-centre (N=14); multiple surgeons (NR)	IPSS, Qmax, duration of catheterisation, QoL, LoS, readmission, blood loss, capsular perforation, complications. ☑	High-risk (includes patients with indwelling catheter, prostate volume >100ml, and patients taking antiplatelet or anticoagulation therapy, but not exclusively).
Reimann *et al.* (2019) Germany	Retrospective non-randomised (n=254) Intervention: GreenLight XPS 180 W PVP (n=140) ☑ Comparator: TURP (n=114) ☑	Patients who underwent PVP or TURP for symptomatic BPE between June 2010 and February 2015. Patients included if they participated in postoperative follow-up. ☑ Setting: single centre; multiple surgeons (NR)	LoS, prolonged hospital stay (>2 days PVP, >4 days TURP), catheterisation duration, complications (<30, 30-180, and >180 days) reintervention, patient satisfaction, IPSS-QoL ☑	High-risk (patients taking anticoagulation and with urine retention, but not exclusively)

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Mathieu *et al.* (2017) France	Retrospective non-randomised (n=237) Intervention: GreenLight XPS 180 W (n=51), monopolar TURP (n=99), HoLEP or ThuLEP (n=64), open prostatectomy (n=23) ☒☑	Data from 20-30 consecutive patients undergoing surgical treatment for LUTS related to BPH (following EAU guidelines) between January 2012 and June 2013 were included. Exclusion criteria: neurogenic bladder, past history of urethral stricture or prostate cancer. ☑ Setting: multi-centre (N=9) included 2 private centres, multiple surgeons (NR)	LoS, readmission, complications, costs ☑	High-risk (includes patients with prostate volume >100ml, urinary retention with catheter preoperatively, and those taking antiplatelet or anticoagulation, but not exclusively). Table 1 identifies multiple surgeons per site, not exclusively identified. Some comparators (ThuLEP combined with HoLEP, open prostatectomy) out scope.
Gondran-Tellier *et al.* (2021) France	Retrospective non-randomised (n=171) Intervention: 180 W PVP, assumed GreenLight XPS (n=62), - monopolar or bipolar TURP (n=48), - endoscopic enucleation via GreenLEP 80 W or HoLEP (n=21), - prostate artery embolisation (n=15), - open prostatectomy (n=25) ☒☑	Patients with refractory urinary retention despite the use of α-blocker and trial without catheter who underwent surgery for BPO between January 2017 and January 2019. All patients had preoperative urinary catheter. Exclusion criteria: neurogenic bladder, prostate cancer, urethral stricture, <12months of clinical follow-up data. ☑ Setting: multi-centre (N=3), multiple surgeons (NR)	LoS, success of catheter removal, catheter-free survival, retention recurrence, reoperation, complications ☑	High-risk (all patients have retention, also includes patients with prostate volume >100ml and patients taking anti-thrombotics but not exclusively) Some comparators (GreenLEP combined with HoLEP, prostate artery embolization, open prostatectomy) out scope.

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Mesnard *et al.* (2021) France	Retrospective non-randomised (n=13) Intervention: GreenLight PVP XPS 180 W, TURP, prostatectomy ☒☑	Patients with haemophilia A or haemophilia B listed in database, who underwent prostate interventions (prostate biopsy, radical prostatectomy, radiotherapy, simple prostatectomy, TURP, GreenLight PVP) between 1st January 1997 and 1st September 2020. Exclusion criteria: age less than 18 years, unknown bleeding disorder at time of surgery, follow-up less than 30 days post-operation. ☑ Setting: single centre; surgeons (NR)	Blood loss, complications, LoS, duration of catheterisation, readmission ☑	High-risk (exclusively in haemophilia patient group).

Key: ☑ aspect of study in scope; ☒ aspect of study not in scope; ☑☒ aspect of study partially in scope, or elements of this are not in scope; † assumed from author affiliations (not explicitly stated in paper).

Abbreviations: AAT, antithrombotic therapy; aPVP, anatomical photoselective vaporisation of prostate; ASA, American Society Anesthesiology; BCI, bladder contractility index; BMI, body mass index; BOO, bladder outlet obstruction; BPH, benign prostatic hyperplasia; BPO, benign prostatic obstruction; DUA, detrusor underactivity; EAC, external assessment centre; Hb, haemoglobin; Ht, haematocrit; IIEF-5, International Index of Erectile Function; IIEF-15, International Index of Erectile Function-15; IPSS, international prostate symptom score; ISI, incontinence severity index; LoS, length of stay; LUTS, lower urinary tract symptoms; MSHQ-EjD, Male Sexual Health Questionnaire; NR, not reported; RCT, randomised controlled trial; PEBE, photoselective en-bloc enucleation; PGI-I, patient global impression of improvement; PSA, prostate specific antigen; PVP, photoselective vaporisation of prostate; PVR, post-void residual volume; QoL, quality of life; SHIM, sexual health inventory for men; TRUS, transrectal ultrasound; TURP, transurethral resection of the prostate; UDS, urodynamic study; UTI, urinary tract infection; VAS, visual analogue scale.

Table 3b: Studies selected by the EAC as the evidence base: studies reporting by high-risk group or setting exclusively (N=9)

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Campobasso *et al.* (2020) †Italy	Retrospective cohort; database (n=1,031) Intervention: GreenLight XPS 180 W; standard PVP (n=550), anatomical PVP (n=481) according to surgeon's preference ☑	Patients undergoing anatomical or standard PVP collected in database between September 2011 and October 2018. Exclusion criteria: history of prostate cancer, neurogenic bladder, previous prostate surgery including GreenLEP or contemporary urethrotomy, treatment of bladder stones and with incidental bladder tumours. Patients were subgrouped by prostate size (<100ml, ≥100ml). ☑ Setting: Multi-centre (NR); multiple surgeons (NR)	Changes in IPSS, PGI-I, Qmax and PSA levels were recorded. Intraoperative outcomes reported: laser time, energy used, duration of catheterisation, surgery duration and complications. LoS, readmission and re-treatment rates were also reported. ☑	High risk (subgrouped by prostate size <100cc and ≥100cc). Patients with antiplatelet & anticoagulant therapy, also patients with indwelling catheter history included, but not exclusively. Includes anatomical vaporisation (but results not reported separately). Despite explicit exclusion of GreenLEP enucleation, presence of mixed terminology: "the dissection is accompanied by vaporization of the enucleated tissue". *Potential overlap with Reale et al. 2020; likely subset of Campobasso et al. 2021; but unconfirmed*.

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Meskawi *et al.* (2017) Canada, France, USA	Retrospective cohort (n=438) Intervention: GreenLight XPS 180 W PVP (n=438) ☑	Patients undergoing GreenLight XPS 180 W PVP for BPH between 2010 and 2015. Treatment indications in accordance with national guidelines. Only patients with prostate volume greater than 100ml on TRUS were included. Patients with prostate cancer or missing pre-operative characteristics were excluded. ☑ Setting: multi-centre (N=8); multiple surgeons (NR)	IPSS, Qmax, QoL, PVR, PSA, retreatment rates, complications, capsular perforation, conversion to TURP, failure to remove catheter, hospital stay. ☑	High-risk (**all** patients have prostate volume greater than 100ml, however also includes patients taking anticoagulants and with history of urinary retention included but not exclusively). Vaporisation procedure starts at 80 W, adjusted in 10-20 W steps up to maximum of 180 W.
Meskawi *et al.* (2019) Location not specified. †Canada/USA/France	Retrospective cohort (n=422) Intervention: GreenLight XPS 180 W PVP, stratified by medication: without antithrombotic agents (control, n=274), acetylsalicylic acid (n=87), other antiplatelets other than acetylsalicylic acid (n=24), anticoagulants (n=37). ☑	Patients treated with GreenLight XPS 180 W PVP for symptomatic BPH between 2011 and 2016. Treatment indications in accordance with American, Canadian and European clinical practice guidelines. Exclusion criteria: unknown coagulation status, GreenLight HPS 120 W used. ☑ Setting: single centre (tertiary medical centre); 1 (high-volume) surgeon	Complications, readmissions, bleeding, LoS, duration of catheterisation, IPSS, Qmax, PVR, retreatment. ☑	High-risk (comparison of patients on no anithrombotic agents, acetylsalicylic acid, antiplatelet agents - other than acetylsalicylic acid, anticoagulation, also includes patients with prostate volume>100ml but not exclusively). Medication was generally stopped prior to surgery and resumed within 24hr. *Potential overlap with Meskawi et al. (2017); unconfirmed*

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Lee *et al.* (2016) USA & Switzerland	Retrospective cohort (n=384) Intervention: GreenLight XPS 180 W PVP; stratified by patients taking anticoagulation (n=186) and those not (n=198) ☑	Patients undergoing GreenLight XPS 180 W PVP for bladder outlet obstruction secondary to BPH between 2010 to 2013. ☑ Setting: multi-centre (N=2); multiple surgeons (NR)	LoS, transfusion, duration of catheterisation, IPSS, PVR, Qmax, PSA, complications, conversion to TURP. ☑	High-risk (cohort stratified into those on anticoagulation and those not, includes patients with prostate volume >100ml in both subgroups but not exclusively).
Waters *et al.* (2021) Ireland	Retrospective cohort (n=374) Intervention: GreenLight XPS PVP ☑	Patients at high risk of bleeding, those with prostate size greater than 80 ml, preoperative urinary retention, or aged greater than 80 years of age. ☑ Setting: multicentre (N=2); 1 surgeon	LoS, adverse events, readmission, blood transfusions, conversion to TURP, catheterisation. ☑	High-risk (all cohort have at least one high risk factor).
Knapp *et al.* (2017) Australia	Retrospective cohort, database (n=373) Intervention: GreenLight XPS 180 W PVP stratified by medication: anticoagulation (heparin, warfarin, clopidogrel, dipyridamole, NOAC, n=59), aspirin (n=42) and patient without aspirin or anticoagulation (n=272) ☑	Patients undergoing PVP between July 2010 and December 2016. ☑ Setting: single centre; 1 surgeon	Duration of catheterisation, LoS, complications, blood transfusion. ☑	High-risk comparison with/without anticoagulant treatments (also includes patients with retention, and patients with prostate volume >100ml but not exclusively).

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Goueli *et al.* (2017) †Canada/USA	Retrospective cohort (n=332) Intervention: GreenLight 180 W XPS PVP; stratified into patients with pre-operative retention (permanent or intermittent urinary catheterisation, (n=137) or without (n=195). ☑	Patients treated with PVP for BPH between 2011 and 2017, in accordance with American and Canadian clinical practice guidelines. Exclusion criteria: prostate cancer, prior radiation, GreenLight HPS 120 W, previous BPH surgery. ☑ Setting: single-centre (authors report majority of surgeries were conducted as an outpatient procedure but this is unquantified); single surgeon.	Hospital stay, duration of catheterisation, blood transfusion, conversion to TURP, complications within 30 and 90 days, IPSS, QoL, Qmax and PVR followed up to 24 months. ☑	High-risk (comparison of patients with and without urinary retention, includes patients taking anticoagulation, prostate volume >100ml and those with history of neurological disease but not exclusively). *Potential overlap with Meskawi et al. (2017) and Pierce et al. (2021); unconfirmed*
Xu *et al.* (2021) China	Retrospective cohort (n=312) Intervention: GreenLight XPS 180 W PVP; stratified as day-case (n=114) or inpatient surgery (n=198) as day-case (n=114). ☑	Patients who underwent GreenLight PVP as a day-case or inpatient procedure for relief of LUTS secondary to BPH between April 2017 and March 2020. Exclusion criteria: anticoagulant dysfunction, cardiopulmonary insufficiency, prostate cancer, bladder tumours, urethral strictures, uncontrolled UTIs, prostate volume >100ml. Additional exclusion criteria listed: neurogenic bladder, diagnosis of prostate or bladder cancer, urethral stricture, serious cardiopulmonary disorders (ASA≥3), prostate volume >120ml. ☑ Setting: single centre; multiple surgeons (NR)	LoS, duration of catheterisation, complications, blood transfusion, TUR, IPSS, QoL, Qmax. ☑	Comparison of day-case and inpatient outcomes. Study reports on cost between arms. EAC assumes additional exclusions were applied to the inpatient group only (although uncertainty over exclusions based on prostate volume).

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Eken & Soyupak (2018) Turkey	Retrospective cohort (n=233) Intervention: GreenLight XPS 180 W PVP stratified by anticoagulation status; anticoagulant (for example aspirin, warfarin sodium, clopidogrel, (n=59) and no anticoagulant (n=174) ☑	Consecutive patients undergoing GreenLight XPS 180 W PVP for treatment of LUTS associated with BPH between November 2012 and October 2016. Indications for surgery in line with EUA (Qmax <15 ml/s, PVR>100ml, IPSS>7). Exclusion criteria: patients with prostate cancer, voiding disorder, neurological diseases (*e.g.* Parkinson's). ☑ Setting: Single centre, 2 surgeons	Conversion to TURP, death, duration of catheterisation, dysuria, reoperation, transfusion, change in IPSS, Qmax, PVR, prostate volume, PSA ☑	High-risk (results reported for subgroup of patients taking anticoagulation separately). Anticoagulants were stopped 3 days prior to surgery with heparin used during interim.

Key: ☑ aspect of study in scope; ☒ aspect of study not in scope ☑☒ aspect of study partially in scope, or elements of this are not in scope; † assumed from author affiliations (not explicitly stated in paper).

Abbreviations: AAT, antithrombotic therapy; aPVP, anatomical photoselective vaporisation of prostate; ASA, American Society Anesthesiology; BCI, bladder contractility index; BMI, body mass index; BOO, bladder outlet obstruction; BPH, benign prostatic hyperplasia; BPO, benign prostatic obstruction; DUA, detrusor underactivity; EAC, external assessment centre; Hb, haemoglobin; Ht, haematocrit; IIEF-5, International Index of Erectile Function; IIEF-15, International Index of Erectile Function-15; IPSS, international prostate symptom score; ISI, incontinence severity index; LoS, length of stay; LUTS, lower urinary tract symptoms; MSHQ-EjD, Male Sexual Health Questionnaire; NR, not reported; RCT, randomised controlled trial; PEBE, photoselective en-bloc enucleation; PGI-I, patient global impression of improvement; PSA, prostate specific antigen; PVP, photoselective vaporisation of prostate; PVR, post-void residual volume; QoL, quality of life; SHIM, sexual health inventory for men; TRUS, trans-rectal ultrasound; TURP, transurethral resection of the prostate; UDS, urodynamic study; UTI, urinary tract infection; VAS, visual analogue scale.

Table 3c: Studies selected by the EAC as the evidence base: single-arm studies reporting on rare adverse events or day-case (N=17)

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Law *et al.* (2021) Canada, France, Germany, Italy, Mexico, Brazil and Argentina	Retrospective cohort; database (n=3,627) Intervention: GreenLight XPS 180 W PVP. ☑	Patients with LUTS secondary to BPH undergoing GreenLight PVP between February 2011 and October 2019. Indication for surgery in respective countries were based on CUA, AUA and EAU guidelines. Exclusion criteria: history of prostate cancer, previous TURP, pelvic radiation, neurological disorders. ☑ Setting: multi-centre (N=7); 8 surgeons	Operative time, LoS, duration of catheterisation, Clavien-Dindo complications. PSA, IPSS, QoL, Qmax, PVR recorded at 3, 6, 12, 24, 36, 48 & 60 months according to local surgeon or clinical preference. ☑	High-risk (34.3% of patients were receiving antithrombotic therapy other than aspirin, 28.5% had ASA score of 3 or higher, and 16.3% patients with prostate volume >100ml but not exclusively).

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Gasmi *et al.* (2021) †France, Spain	Propensity matched cohort, sampled from prospective database (n=2,420) Intervention: GreenLight 120 W laser enucleation of the prostate with HPS 2090 fibre (GreenLEP) (total=929, n=78 propensity matched) ☒ Comparator: GreenLight PVP 180 W XPS (total 1,491, n=78 propensity matched) ☑	Consecutive patients diagnosed with LUTS due to BPO, who underwent GreenLight laser surgery (PVP or GreenLEP) between April 2011 and April 2020. Exclusion criteria: neurological disease, previous urethral stricture, history of prostate cancer or prostate surgery. Concomitant surgical procedures were excluded. ☑ Setting: Multi-centre; multiple surgeons (NR)	Peri-operative variables: operative time, energy used, complications, conversion to another procedure, blood loss, LoS. IPSS, Qmax, PVR, PSA and UTI reported. ☑	Patients propensity matched using age, ASA, prostate volume, PSA, antiplatelet/anticoagulant therapy, baseline IPSS, indwelling catheter, baseline Qmax, PVR, year of surgery, surgeon's experience. Matched 1:1 without replacement using nearest-neighbour matching. Comparison of GreenLight and GreenLEP (comparator out of scope 120 W with HPS fibre, treat as prospective cohort with 1491 patients).
Rajih *et al.* (2017) Canada, US	Retrospective cohort (n=941) Intervention: GreenLight XPS 180 W, patients stratified by risk groups based on ASA status; high risk ASA≥3, low risk ASA≤2. ☒☑	Patients diagnosed with LUTS secondary to BPH undergoing GreenLight XPS PVP (indications based on CUA, AUA and EAU guidelines) from August 2010 and August 2014. Exclusion criteria: prostate cancer, previous radiation therapy, neurological disease, urethral stricture or urinary incontinence prior to surgery. ☑ Setting: multi-centre (N=5); multiple surgeons (NR)	IPSS, Qmax, PVR, duration of catheterisation, QoL, LoS, readmission, blood loss, capsular perforation, adverse events. ☑	High-risk (both low and high risk groups as defined by ASA include patients with prostate volume >100ml, taking anticoagulation, and with urinary retention, but not exclusively). Short term outcomes: 6 months)

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Trujillo *et al.* (2021) Columbia	Retrospective cohort (n=587) Intervention: GreenLight XPS 180 W PVP stratified into prostate volume <80ml (n=381), ≥80ml (n=206) ☒☑	Patients who underwent PVP for relief of LUTS secondary to BPE between 2012 and 2019. Only patients with insufficient data to meet outcomes were excluded (assume 253 patients with missing data) ☑ Setting: single centre, multiple surgeons (NR).	PSA, IPSS, QoL, SHIM, patient satisfaction using VAS, catheterisation, LoS, Qmax, PVR. Intraoperative variables: operation time, energy applied, energy density, bleeding, conversion rates, catheterisation time, hospital stay. ☑	Subgroups by prostate volume (dichotomised into <80ml and ≥80ml); high-risk (includes patients with history of anticoagulation and urine retention, and prostate volume >100ml but not exclusively). 80 W starting power increasing to 180 W. *Potential overlap with Barco-Costillo et al. (2020); although not explicitly confirmed.*
Trail *et al.* (2021) UK	Retrospective cohort (n=538) Intervention: GreenLight XPS 180 W PVP; subgroups include day-case (n=366) and non-day-case (n=172) ☑	Patients who underwent GreenLight PVP between October 2016 and June 2021 inclusive. Exclusion criteria: GreenLight PVP on NHS operating lists undertaken in private healthcare institutions, revision GreenLight PVP. ☑ Setting: single centre; 7 surgeons	Qmax, PVR, patient satisfaction, reoperation, LoS, readmission, day-case procedures, conversion to TURP, operation time, laser time, energy used, duration of catheterisation, complications. ☑	High-risk (includes patients with urinary retention but not exclusively) Subgroup analysis includes day-case versus admissions. Discussion of cost implications for NHS reported.

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Castellucci *et al.* (2020) †Italy	Retrospective cohort, database (n=487) Intervention: GreenLight XPS 180 W PVP, subgroup by those undergoing concomitant procedure (n=58, of which 29 were endoscopic and 29 were open/laparoscopic procedures) and those undergoing GreenLight PVP alone (n=429) ☒☑	Patients undergoing PVP to relieve LUTS/BPH symptoms extracted from database 2011-2016. No exclusion criteria reported. ☑ Setting: multi-centre (NR); multiple surgeons (NR)	Changes with IPSS, Qmax, PSA, laser time, energy used, complications, retention, capsule perforation, LoS, satisfaction. ☑	High-risk (includes patients with history of catheterisation, and also includes patients with ASA III and IV, but not exclusively).
Reimann *et al.* (2018) Germany	Retrospective cohort (n=375) Intervention: GreenLight XPS 180 W ☑	Patients undergoing GreenLight for symptomatic BPH between June 2010 and February 2015. Exclusion criteria: none listed. ☑ Setting: single centre; 5 surgeons	Duration of catheterisation, PSA, dysuria, QoL, LoS, blood loss, TUR syndrome, readmission, retreatment, complications. ☑	High risk (reports volume of urinary retention and includes patients taking anticoagulation, but not exclusively). Reports differences over time (annually between 2010-2015).
Zhou *et al.* (2017) Canada	Retrospective cohort (n=328) Intervention: GreenLight 180 W XPS PVP ☑	Patients undergoing GreenLight PVP. Exclusion criteria: patients diagnosed with prostate cancer were excluded. ☑ Setting: single centre (tertriary centre); 1 surgeon	IPSS, Qmax, PVR, PSA, duration of catheterisation, QoL, LoS, day-case, readmission, blood loss, capsular perforation. ☑	High-risk (patients taking anticoagulation, but not exclusively). Assessing learning curve.

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Ghahhari *et al.* (2021) †Italy	Prospective cohort (n=193) Intervention: Standard and anatomic GreenLight XPS 180 W PVP (subgrouped by chronic use, >6 months, of 5ARI (n=87) and those not receiving 5ARI (n=106)) ☒☑	Patients undergoing GreenLight XPS PVP between February 2017 and September 2019, for relief of LUTS. Inclusion criteria: IPSS ≥12, or QoL ≥4, or Qmax <15mL, or no improvement with medical therapy, or unwilling to undergo medical therapy. Exclusion criteria: history of prostatic or urethral surgery, urethral stricture, neuro-vesical dysfunction, prostate cancer. ☑ Setting: multi-centre (N=2), single surgeon	Laser efficiency (energy density, vaporisation efficiency, vaporisation power), early complications (within 30 days post-op), late complications (after 90 days post-op), storage symptoms (pollakiuria, dysuria, urgency), re-intervention, urinary incontinence, quality of life via Patient Global Impression of Improvement (PGI-I), IPSS, Qmax, PSA, catheterisation duration, LoS.☑	Mixture of standard PVP (58%) and anatomical vaporisation (42%).
Liu *et al.* (2020) China	Retrospective cohort (n=150) Intervention: GreenLight XPS 180 W ☑	Patients with LUTS secondary to BPH undergoing PVP between January 2016 and October 2018. No exclusion crietria reported. ☑ Setting: single centre; 1 surgeon	IPSS, change in prostate volume, Qmax, PVR, duration of catheterisation, dysuria, QoL, LoS, readmissions, blood loss, TUR syndrome, capsular performation, complications.☑	High-risk (includes patients with prostate volume >100ml, and those taking anticoagulation, but not exclusively)
Ghahhari *et al.* (2018) †Italy	Retrospective cohort (n=140) Intervention: GreenLight XPS including standard PVP, anatomical PVP or PEBE (choice of surgeon) ☒☑	Patients undergoing GreenLight PVP between February 2013 and April 2017. Exclusion criteria: patients missing preoperative characteristics (not defined). ☑ Setting: single centre; 1 surgeon	IPSS, Qmax, duration of catheterisation, LoS, readmission, blood loss, capsular perforation, complication. ☑	High-risk (includes patietns with urinary retention and patients taking anticoagulation, but not exclusively).

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Berquet *et al.* (2015) France	Prospective cohort (n=134) Intervention: GreenLight XPS 180 W PVP ☑	Patients undergoing GreenLight PVP in ambulatory care (day-case) between May 2012 and June 2013. All patients had LUTS related to BPH, indications for surgery based on EAU guidelines or the French Association of Urology. Exclusion criteria: neurogenic bladder, patients taking anti-vitamin K, history of urethral stricture, ASA >3, age >80y, social status unsuited for ambulatory care procedure (living alone or >1h from hospital). Those with urethral catheter or taking platelet aggregation inhibitors were not excluded. ☑ Setting: multi-centre (N=2), ambulatory Care	Changes in Qmax, PVR, IPSS and IPSS QoL at 3 months postoperatively and compared according to prostate size subgroups (≤40ml; 41-79ml; ≥80ml). Patient satisfaction relating to undergoing procedure in an ambulatory care setting was reported. Intraoperative outcomes reported: laser time, energy, surgery duration and complications within 30 days. LoS and readmissions were also reported. ☑	Information regarding day-case PVP procedure. Includes one university hospital and private hospital. Includes high-risk patients (clopidogrel).
Tao *et al.* (2019) China	Prospective cohort (n=102) Intervention: GreenLight XPS 180 W ☑	Patients undergoing laser vaporisation for LUTS secondary to BPH, between April 2017 and April 2018. Surgical indications in line with Chinese Urological Assocation guidelines, Qmax <15 ml/s, and IPSS ≥8. Exclusion criteria: neurogenic bladder, diagnosis of prostate orbladder cancer, urethral stricture. ☑ Setting: multi-centre (N=NR); multiple surgeons (N=3)	IPSS, change in prostate volume, Qmax, QoL PVR, duration of catheterisation, LoS, readmission, blood loss, TUR syndrome, capsular perforation, complications. ☑	High-risk (includes patients with prostate volume >100ml, patients with urine retention, and patients taking anticoagulation, but not exclusively).

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Aboutaleb *et al.* (2018) †Egypt, United Arab Emirates	Retrospective cohort (n=155) Intervention: GreenLight XPS 180 W (n=75) ☑ Comparator: Bipolar plasma vaporisation (n=80) ☒	Patients with BPH enrolled between March 2012 and January 2017. Inclusion criteria: age >50 years, prostate volume 30-100 ml, serum PSA <2.5 ng/ml, IPSS ≥20, Qmax ≤ 10ml/s and failed medical therapy for BPH. Exclusion criteria: abnormal digital rectal exam or ultrasonography with suspicion of prostate cancer, history of prostate cancer, previous urethral or prostate surgery, urethral stricture, neurogenic bladder, bladder neck sclerosis, bladder calculi, BPH-related hydronephrosis, active urinary tract infections, renal insufficienct, previous myocardial infarction within 6 monhts, previous TURP, serum creatinine >200 mol/l. ☑ Setting: centres (NR); 4 surgeons	IPSS, Qmax, PVR, duration of catheterisation, QoL, LoS, blood loss, capsular perforation, complications. ☑	Comparator out of scope, treat as single-arm study.

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Chen and Chiang (2016) Taiwan	Retrospective cohort (n=65) Intervention: GreenLight 180 W XPS ☑ Comparator: GreenLight 120 W HPS ☒	Patients with LUTS secondary to BPH undergoing treatment with GreenLight 120 W HPS (August 2008 to September 2009) or GreenLight 180 W XPS (September 2014 to September 2015). All patients showed poor response to alpha-blocker or 5ARI. Indications for surgery based on European guidelines. Exclusion criteria: prior urethral sugery, suspected neurogenic bladder, prostate cancer. ☑ Setting: single centre; 1 surgeon.	IPSS, change in prostate volume, Qmax, PVR, duration of catheterisation, dysuria, QoL, LoS, readmission, blood loss, TUR syndrome, complications. ☑	Comparator out of scope, treated as single arm.
Thomas *et al.* (2019) †Canada, US	Retrospective cohort (n=58) Intervention: GreenLight XPS 180 W; anatomical vaporisation. ☑	Patients treated with GreenLight PVP for BOO between 2012 and 2016. Only patients with small volume prostates (<40ml) were included. All treatment indications in line with American and Canadian guidelines. Exclusion criteria: history of prostate cancer, radiation therapy, chronic retention ☑ Setting: multi-centre (N=2 tertiary medical centres); multiple surgeons (NR)	IPSS, Qmax, PVR, QoL, LoS, capsular perforation, complications. ☑	High-risk (includes patients with urine retention and those taking antithrombotic therapies, but not exclusively). Patients with prostate volumes <40 ml

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Ferrari *et al.* (2021b) Italy	Prospective cohort (n=10) Intervention: GreenLight XPS 180 W ☑	Patients treated with GreenLight PVP for BPO between July 2019 and September 2019. All patients who had PSA >4 ng/ml, abnormalities in digital rectal examination, or PIRADS lesions ≥3 at multiparametric MRI underwent randomised and targeted ultrasound-guided biopsies before surgery. Exclusion criteria: history of prostate cancer, previous prostate surgery, simultaneous urethrotomy, treatment or bladder stones, and bladder tumours. ☑☒ Setting: single-centre, 2 surgeons	Analysis of chemical composition of the surgical smoke and outflow irrigation fluid (rare adverse event, device related) ☑☒	Included for rare device-related adverse events only.

Key: ☑ aspect of study in scope; ☒ aspect of study not in scope ☑☒ aspect of study partially in scope, or elements of this are not in scope; †Assumed from author affiliations (not explicitly stated in paper).

Abbreviations: AAT, antithrombotic therapy; aPVP, anatomical photoselective vaporisation of prostate; ASA, American Society Anesthesiology; BCI, bladder contractility index; BMI, body mass index; BOO, bladder outlet obstruction; BPH, benign prostatic hyperplasia; BPO, benign prostatic obstruction; DUA, detrusor underactivity; EAC, external assessment centre; Hb, haemoglobin; Ht, haematocrit; IIEF-5, International Index of Erectile Function; IIEF-15, International Index of Erectile Function-15; IPSS, international prostate symptom score; ISI, incontinence severity index; LoS, length of stay; LUTS, lower urinary tract symptoms; MSHQ-EjD, Male Sexual Health Questionnaire; NR, not reported; RCT, randomised controlled trial; PEBE, photoselective en-bloc enucleation; PGI-I, patient global impression of improvement; PSA, prostate specific antigen; PVP, photoselective vaporisation of prostate; PVR, post-void residual volume; QoL, quality of life; SHIM, sexual health inventory for men; TRUS, trans-rectal ultrasound; TURP, transurethral resection of the prostate; UDS, urodynamic study; UTI, urinary tract infection; VAS, visual analogue scale.

5 Clinical evidence review

5.1 *Overview of methodologies of all included studies*

A total of 37 studies included by the EAC comprised of:

- 1 RCT (Abolazm *et al.* 2020),
- 3 propensity matched cohorts (Azizi *et al.* 2017; Castellani *et al.* 2018; Cimino *et al.* 2017),
- 7 non-randomised, non propensity-matched comparative studies (Cindolo *et al.* 2017; Gondran-Tellier *et al.* 2021; Hibon *et al.* 2017; Mathieu *et al.* 2017; Mattevi *et al.* 2020; Mesnard *et al.* 2021; Reimann *et al.* 2019;),
- 9 cohort studies stratified by risk groups and reported their outcomes separately (Campobasso *et al.* 2020; Eken and Soyupak 2018; Goueli *et al.* 2017; Knapp *et al.* 2017; Lee *et al.* 2016; Meskawi *et al.* 2019, Meskawi *et al.* 2017; Waters *et al.* 2021; Xu *et al.* 2021),
- 17 single-arm studies, which reported on rare adverse events (TUR syndrome, capsular perforation and device-related adverse events) or day-case procedures (Aboutaleb *et al.* 2018; Berquet *et al.* 2015; Castellucci *et al.* 2020; Chen and Chiang 2016; Ferrari *et al.* 2021b; Gasmi *et al.* 2021; Ghahhari *et al.* 2021; Ghahhari *et al.* 2018; Law *et al.* 2021; Liu *et al.* 2020; Rajih *et al.* 2017; Reimann *et al.* 2018; Tao *et al.* 2019; Thomas *et al.* 2019; Trail *et al.* 2021; Trujilo *et al.* 2021; Zhou *et al.* 2017).

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

One randomised controlled trial was identified and critically appraised using the Cochrane Collaboration's tool for assessing risk of bias in randomised trials (Higgins *et al.* 2011), Appendix B1. The study (Abolazm *et al.* 2020) was deemed high-quality, however the study compared two different surgical techniques, both using the Greenlight XPS (ejaculatory hood sparing PVP

versus standard PVP) and therefore not directly relevant to the decision problem.

Seven non-randomised comparative studies (five retrospective and two prospective in nature) were identified and critically appraised using the Joanna Briggs Institute Checklist for Quasi-Experimental Studies tool, Appendix B2. Three compared PVP with TURP (Mesnard *et al.* 2021; Mattevi *et al.* 2020; Reimann *et al.* 2019). Two compared standard PVP with anatomical PVP (Cindolo *et al.* 2017; Hibon *et al.* 2017). Two compared PVP with multiple surgical techniques; Mathieu *et al.* (2017) compared GreenLight PVP with monopolar TURP, open prostatectomy and HoLEP or ThuLEP; Gondran-Tellier *et al.* (2021) compared GreenLight PVP with mono- and bi-polar TURP, enucleation (using GreenLEP or HoLEP), prostate artery embolisation and open prostatectomy.

Three propensity matched cohorts and nine cohort studies were identified and critically appraised using the NIH National Heart, Lung and Blood Institute Cohort tool, Appendix B3. The three propensity matched cohorts each compared GreenLight PVP with a different comparator: Cimino *et al.* (2017) compared GreenLight PVP with TURP, Castellani *et al.* (2018) with ThuVEP, and Azizi *et al.* (2017) with GreenLight vaporincision (also described as vaporesection). Definition of high-risk patients varied across studies (*e.g.* ASA category, BMI, age threshold, prostate volume greater than 80 ml), however high-risk in the context of the remainder of the report focuses on the definition in the decision problem of the NICE Final Scope (NICE MT564 Final Scope, 2021). Four cohort studies stratified patients by anticoagulation status:

- Meskawi *et al.* (2019) subgrouped into aspirin, antiplatelet other than aspirin or combinations with aspirin, anticoagulant, no anticoagulant or antiplatelet medication;
- Eken and Soyupak (2018) defined an anticoagulation group as patients taking aspirin, warfarin or clopidogrel, compared with patients on no anticoagulation;

- Knapp *et al.* (2017) subgrouped into an anticoagulation group included heparin, warfarin, clopidogrel, dipyridamole or DOAC medications, compared with patients taking aspirin exclusively, and those with no anticoagulant or aspirin;

- Lee *et al.* (2016) which defined an anticoagulation group as those taking aspirin, clopidogrel and warfarin, compared with patients taking no anticoagulant.

One study, Goueli *et al.* (2017), stratified by presence of preoperative urine retention (permenant or intermittent combined). One study stratified by prostate volume; Campobasso *et al.* (2020) (less than 100 ml, or 100 ml and greater). One stratified by procedure setting; Xu *et al.* (2021) (day-case, inpatients). One cohort study was conducted exclusively in patients with prostate volume greater than 100 ml (Meskawi *et al.* 2017), and one study reported results from a cohort of patients with at least one risk factor; high risk of bleeding, prostate volume greater than 80 ml, preoperative retention or aged greater than 80 years (Waters *et al.* 2021).

Seventeen single-arm studies (study size ranging from 10 to 3,627 patients) were only included in the EAC review due to their reporting on rare adverse events; two single-arm studies were included due to their reporting of day-case GreenLight procedures; Appendix B3.

Four studies were set in more than one country and included at least one European centre (Law *et al.* 2021; Meskawi *et al.* 2019; Meskawi *et al.* 2017; Lee *et al.* 2016). Twenty studies were conducted exclusively in European countries, including:

- nine in Italy (Campobasso *et al.* 2020; Castellani *et al.* 2018; Castellucci *et al.* 2020; Cimino *et al.* 2017; Cindolo *et al.* 2017; Ghahhari *et al.* 2021; Ghahhari *et al.* 2018; Mattevi *et al.* 2020; Ferrari *et al.* 2021b);

- five in France (Berquet *et al.* 2015; Gondran-Tellier *et al.* 2021; Hibon *et al.* 2017; Mathieu *et al.* 2017; Mesnard *et al.* 2021);

- two in Germany (Reimann *et al.* 2019; Reimann *et al.* 2018);
- one in France and Spain (Gasmi *et al.* 2021);
- one in Turkey (Eken and Soyupak 2018);
- one in Ireland (Waters *et al.* 2021);
- one in the UK (Trail *et al.* 2021).

The majority of studies were conducted in a secondary or tertiary care setting. One retrospective cohort study, conducted in the UK, reported outcomes from 538 GreenLight procedures stratified by day-case and non-day-case procedures (Trail *et al.* 2021); one prospective cohort study reported outcomes from 134 patients all treated in an ambulatory care unit in France (Berquet *et al.* 2015); and one study conducted in China stratified a cohort by day-case or inpatient procedure type (Xu *et al.* 2021).

The largest study was a retrospective cohort by Law *et al.* (2021), which used data from the Global GreenLight Group database, reporting on outcomes from 3,627 patients undergoing PVP with the GreenLight XPS 180 W system between 2011 and 2019, with median follow-up of 6 months, and maximum follow-up of 60 months achieved in 129 patients. The retrospective cohort study by Meskawi *et al.* (2019) also achieved followed patients up to 60 months; median 24 (range 3 to 60) months. A number of studies reported lack of follow-up as the main limitation of their study design, explaining that follow-up would routinely be conducted in primary care and records were not available retrospectively from the treating hospital.

5.3 *Results from the evidence base*

Symptoms of BPH (International Prostate Symptom Score, IPSS)

Five comparative studies reported on the severity of symptoms via the Interventional Prostate Symptom Score (IPSS) before and after surgery, including one RCT; in addition to two propensity matched cohort, and two non-randomised comparative studies. Two subgroup analyses also reported on this outcome, including two retrospective cohort studies (one comparing

anticoagulation status, one comparing day-case with inpatient surgery), Table 4.

The propensity matched cohort reported by Cimino *et al.* (2017) reported there was no significant difference in IPSS between GreenLight PVP (n=55) and TURP (n=55) at 3, 6 and 12 months follow-up. The RCT (n=49) by Abolazm *et al.* (2020) reported no significant difference in IPSS total, voiding or storage between standard GreenLight PVP (n=24) and ejaculatory hood sparing GreenLight PVP (n=25) arms at 1, 3, 6 and 12 months follow-up.

Lee *et al.* (2016) reported significant improvements in IPSS scores up to 24 months follow-up, with no difference between presence and absence of systemic anticoagulation. In addition, the study reported that there was no difference between the number of anticoagulants a patient was taking and improvement in IPSS scores (p=0.37). The database reported by Campobasso *et al.* (2020) reported that IPSS was not significantly different at baseline, 6 and 12 months between patients with prostate volume less than 100 ml (n=916) and those not (n=115). However, the study reported that IPSS decrease was larger in those with large prostates over time, p=0.013.

Xu *et al.* (2021) reported significant improvements in IPSS scores at up to 12 month follow-up when compared to baseline measurements, with no statistical comparison between day-case (n=114) and inpatient (n=198) patients.

Castellani *et al.* (2018) reported that the proportion of patients with a reduction in IPSS of 20 or greater at 6 months was significantly different between GreenLight PVP and ThuVEP propensity matched arms (73.3% and 28.9% respectively), and also a significant difference in proportion with a reduction of 21 or greater at 12 months between arms (68.9% and 37.8% respectively).

The propensity matched cohort by Azizi *et al.* (2017) reported a significant difference in mean change in IPSS between GreenLight PVP (n=222) and vaporincision (n=222) arms at six months in favour of the latter GreenLight technique. The non-randomised study by Mattevi *et al.* (2020) found no significant difference in change in IPSS between patients undergoing TURP (n=50) or GreenLight PVP (n=50). Cindolo *et al.* (2017) reported a significant

change in IPSS at six month follow-up with no difference between using the standard (n=410) or anatomical (n=403) GreenLight PVP technique. Two additional studies illustrated the change in IPSS but did not provide numerical values. Goueli *et al.* (2017) stratified a cohort by presence of pre-operative urine retention, and Meskawi *et al.* (2019) stratified a cohort by antithrombotic status (no antithrombotics, aspirin, antiplatelets, anticoagulation); both studies and reported a significant decrease in IPSS compared with baseline *within* each subgroup at all follow-up time points up to 24 months.

Only one study reported on the BPH6 endpoint (composite of six elements: LUTS relief; recovery experience; erectile function; ejaculatory function; continence; safety). The propensity matched cohort by Cimino *et al.* (2017) reported that after 1 year of follow-up that BPH6 recovery was significantly higher in the GreenLight PVP arm when compared to TURP, 45.6% and 18.2%, p=0.001.

Table 4: Comparative studies (N=7) reporting IPSS outcome; reported as either mean (SD), median [IQR] or median {range}

Author (year)	Study design	Timepoint	Arm 1	IPSS	Arm 2	IPSS	p-value
Abolazm *et al.* (2020)†	RCT (n=49)	Baseline 1 month 3 months 6 months 12 months	GreenLight PVP (standard)	25.3 (3.8) NR	GreenLight PVP (ejaculatory hood sparing)	23.5 (3.5) NR	0.089 0.9 0.08 0.6 0.8
Azizi *et al.* (2017)	Propensity matched (n=444)	Baseline 6 months	GreenLight PVP	20.6 6.6	GreenLight vaporincision	22.6 5.6	0.07 0.59
Cimino *et al.* (2017)	Propensity matched (n=110)	Baseline 3 months 6 months 12 months	GreenLight PVP	24.80 (7.72) NR	TURP	24.93 (4.51) NR	0.97 0.45 0.34 0.89
Mattevi *et al.* (2020)	Non-randomised (n=100)	Baseline 1 year	GreenLight PVP	22.2 (5.8) 9.3 (3.0)	TURP	20.1 (5.4) 8.7 (5.1)	0.06 0.58
Cindolo *et al.* (2017)	Non-randomised (n=813)	Baseline 6 months	GreenLight PVP	29 [19 to 27] NR	GreenLight PVP (anatomical)	23 [20 to 27] NR	0.076
Lee *et al.* (2016)	Cohort (n=384)	Baseline 1 month 3 months 6 months 12 months 2 years	GreenLight PVP (no anticoag)	18.5 [14 to 23] 9 [5 to 17] 5.5 [2.5 to 10] 5 [3 to 9] 5 [2 to 7] 7 [5 to 8]	GreenLight PVP (anticoag)	16 [12 to 22] 8 [5 to 13] 5 [3 to 9] 4 [3 to 8] 4 [2 to 7] 4 [4 to 7]	0.09 0.22 0.99 0.72 0.37 0.14
Xu *et al.* (2021)	Cohort (n=312)	Baseline 3 months 6 months 12 months	GreenLight PVP (inpatient)	24.0 (4.4) 11.7 (3.3) 11.6 (3.2) 11.1 (3.0)	GreenLight PVP (day-case)	23.1 (4.5) 12.4 (3.5) 11.8 (3.1) 11.4 (2.8)	0.073 >0.05* >0.05* >0.05*

Abbreviations: RCT, randomised controlled trial; PVP, photoselective vaporisation of the prostate; TURP, transurethral resection of the prostate; NR, not reported

†Intervention (ejaculatory hood sparing GreenLight PVP) and comparator (standard GreenLight PVP) have been swapped in order to be consistent with reporting of other studies
* Comparison between outcome measure at that time point compared to baseline/preoperative measure not a comparison between arms

Change in prostate volume

Only one study reported on change in prostate volume, Table 5; Eken and Soyupak (2018) reported a significant change in prostate volume following surgical intervention after three months follow up. Prostate volume was reported across the aggregated cohort of participants, whilst other study outcomes were otherwise reported by subgroups depending on anticoagulant use or non-use. No significant difference in baseline prostate volume between the groups was reported (p=0.35).

Two studies reported reduction in prostate volume up to 12 months following GreenLight XPS PVP, however no statistical analysis or inference was made (Liu *et al.* 2020; Tao *et al.* 2019). Chen and Chiang (2016) reported a significant change in percentage reduction in prostate volume between patients undergoing PVP using either the GreenLight XPS and GreenLight HPS systems (p=0.0008).

Table 5. Summary of the studies (N=1) reporting in change in prostate volume; reported as mean (SD), median [IQR] or median {range}.

Author (year)	Total no. of patients	Timepoint	Baseline prostate volume ml	Follow-up prostate volume, ml	p-value
Eken and Soyupak (2018)	n=233	3 months	57.2 (19.4)	30.4 (9.1)	<0.05

Maximum flow rate (Qmax)

Five comparative studies reported maximum flow rate, including one RCT, two propensity matched cohorts, and two non-randomised studies. Two subgroup analyses also reported on this outcome, both were retrospective cohort studies (one comparing subgroups based on anticoagulation status, one comparing outcomes of day-case and inpatient surgeries), Table 6.

The RCT (n=49) by Abolazm *et al.* (2020) reported no significant difference in Qmax between standard GreenLight PVP (n=24) and ejaculatory hood sparing GreenLight PVP (n=25) arms at 1, 3, 6 and 12 months follow-up. The authors also reported no significant difference in detrusor pressure reached

during maximum urinary flow (PdetQmax, measured in ml H_2O) post-operatively between arms.

The database reported by Campobasso *et al.* (2020) reported that Qmax was not significantly different between patients with prostate volume less than 100 ml and those not. However, the study reported that the increase in Qmax was larger in those with large prostates, p=0.022. Lee *et al.* (2016) reported a significant improvement in Qmax up to 24 month follow-up, and reported no difference between patients taking anticoagulation (n=186) and those not (n=198).

Xu *et al.* (2021) reported significant improvements in Qmax up to 12 months follow-up when compared to baseline measurements, with no statistical comparison between day-case and inpatient patients. Castellani *et al.* (2018) reported no significant difference in the proportion of patients with an increase in Qmax of 10.5 or greater at 6 months between GreenLight PVP and ThuVEP propensity matched arms (57.8% and 53.3% respectively), but a significant difference in the proportion of patients with an increase in Qmax of 12 or greater at 12 months (64.4% and 33.3% respectively).

The non-randomised study (n=100) by Mattevi *et al.* (2020) reported no significant difference in change in Qmax at 12 months between patients undergoing TURP (n=50) or GreenLight PVP (n=50). Similarly, the propensity matched cohort (n=110) by Cimino *et al.* (2017) found no difference in change in Qmax between GreenLight (n=55) and TURP (n=55) at 3, 6 and 12 months. The propensity matched cohort (n= 444) by Azizi *et al.* (2017) reported a significant difference in change in Qmax between GreenLight PVP (n=222) and GreenLight vaporincision (n=222) arms at 6 months with a higher urinary flow rate in the latter group. Two additional studies illustrated the change in Qmax but did not provide numerical values. Goueli *et al.* (2017) stratified a cohort by presence of pre-operative urine retention, and Meskawi *et al.* (2019) stratified a cohort by antithrombotic status (no antithrombotics, aspirin, antiplatelets, anticoagulation); both studies reported a significant increase in Qmax compared with baseline *within* each subgroup at all follow-up time points up to 24 months.

Table 6: Comparative studies (N=7) reporting change in Qmax; reported as mean (SD), median [IQR] or median {range}

Author (year)	Study design	Timepoint	Intervention	Qmax	Comparator	Qmax	p-value
Abolazm *et al.* (2020)†	RCT (n=49)	Baseline 1 month 3 months 6 months 12 months	GreenLight PVP (standard)	8.7 (3.4) NR NR NR NR	GreenLight PVP (ejac hood paring)	7.9 (3.0) NR NR NR NR	0.3 0.6 0.8 0.3 0.6
Azizi *et al.* (2017)	Propensity matched (n=444)	Baseline 6 months	GreenLight PVP	8.2 17.6	GreenLight vaporincision	7.1 19.9	0.017 0.008
Cimino *et al.* (2017)	Propensity matched (n=110)	Baseline 3 months 6 months 12 months	GreenLight PVP	9.12 (1.92) NR NR NR	TURP	9.06 (2.01) NR NR NR	0.45 0.91 0.49 0.87
Mattevi *et al.* (2020)	Non-randomised (n=100)	Baseline 1 year	GreenLight PVP	8.4 (1.7) 17 (3.0)	TURP	7.6 (3.0) 15.6 (6.4)	0.14 0.15
Cindolo *et al.* (2017)	Non-randomised (n=813)	Baseline 6 months	GreenLight PVP	8.2 [7.0 to 10.0] NR	GreenLight PVP (anatomical)	9.0 [7.0 to 10.9] NR	0.301
Lee *et al.* (2016)	Cohort (n=384)	Baseline 1 month 3 months 6 months 12 months 2 years	GreenLight PVP (no anticoag)	6.3 [3 to 11] 10.9 [6.6 to 18.2] 14.4 [8.6 to 20.3] 12.9 [9.2 to 20.3] 16.6 [9.4 to 20.5] 17.5 [12.6 to 21.3]	GreenLight PVP (anticoag)	8.7 [5.3 to 11.7] 11.2 [6.6 to 18.2] 14.1 [10.6 to 19.3] 18.2 [12.9 to 22.5] 16.5 [11.7 to 22.5] 18.7 [15.6 to 22.3]	0.06 0.73 0.93 0.25 0.87 0.40
Xu *et al.* (2021)	Cohort (n=312)	Baseline 3 months 6 months 12 months	GreenLight PVP (inpatient)	6.9 (2.7) 16.9 (1.8) 17.1 (1.7) 17.3 (1.4)	GreenLight PVP (day-case)	6.7 (2.4) 17.2 (2.0) 17.4 (1.9) 17.5 (1.6)	0.577 >0.05* >0.05* >0.05*

Abbreviations: NR, not reported; PVP, photoselective vaporisation of the prostate; TURP; transurethral resection of the prostate; RCT, randomised controlled trial
†Intervention (ejaculatory hood sparing GreenLight PVP) and comparator (standard GreenLight PVP) have been swapped in order to be consistent with reporting of other studies.
* Comparison between outcome measure at that time point compared to baseline/preoperative measure not a comparison between arms

Post-void residual volume (PVR)

Four comparative studies report on post-void residual volume (PVR), including one RCT, one propensity matched cohort and two retrospective cohort studies (one comparing subgroups defined by anticoagulation status, one comparing outcomes between day-case and inpatient surgeries), Table 7.

No significant difference in PVR was reported in the RCT by Abolazm *et al.* (2020) between standard GreenLight PVP and ejaculatory hood sparing GreenLight PVP arms (if correction for multiple statistical testing had been applied) at 1, 3, 6 and 12 months follow-up.

A significant difference in PVR between GreenLight PVP and GreenLight vaporincision arms was reported by Azizi *et al.* (2017) at six months with a lower PVR reported in the latter technique.

Lee *et al.* (2016) reported a significant improvement in PVR up to 24 months follow-up, with no significant difference between patients taking anticoagulation (n=186) and those not (n=198).

Xu *et al.* (2021) reported significant improvements in PVR up to 12 month follow-up when compared to baseline measurements, with no statistical comparison between day-case and inpatient patients.

Two additional studies illustrated the change in PVR but did not provide numerical values. Goueli *et al.* (2017) stratified a cohort by presence of pre-operative urine retention, and Meskawi *et al.* (2019) stratified a cohort by antithrombotic status (no antithrombotics, aspirin, antiplatelets, anticoagulation); both studies reported a significant decrease in PVR compared with baseline *within* each subgroup at all follow-up time points up to 24 months.

Table 7: Summary of studies (N=4) reporting changed in PVR; reported as mean (SD) or median [IQR]

Author (year)	Study design	Timepoint	Intervention	Post-operative PVR	Comparator	Post-operative PVR	p-value
Abolazm *et al.* (2020)†	RCT (n=49)	Baseline 1month 3months 6months 12months	GreenLight PVP	22 [0-240] NR NR NR NR	GreenLight PVP (ejac hood sparing)	26 [0-300] NR NR NR NR	0.5 0.8 0.04 0.8 0.4
Azizi *et al.* (2017)	Propensity matched (n=444)	Baseline 6months	GreenLight PVP	221 55	GreenLight vaporincision	255 26	0.24 <0.001
Lee *et al.* (2016)	Cohort (n=384)	Baseline 1 month 3 months 6 months 12 months 2 years	GreenLight PVP (no anticoag)	100 [50 to 250] 39.5 [0 to 98] 16 [0 to 49] 25 [0 to 55] 20 [0 to 55] 10 [0 to 50]	GreenLight PVP (anticoag)	95.5 [50 to 150] 37 [0 to 110] 2 [0 to 52] 0 [0 to 55] 10 [0 to 46] 0 [0 to 45]	0.02 0.62 0.98 0.66 0.58 0.43
Xu *et al. (*2021)	Cohort (n=312)	Baseline 3 months 6 months 12 months	GreenLight PVP (inpatient)	126 (76.8) 16.6 (18.1) 17.0 (16.3) 17.3 (16.6)	GreenLight PVP (day-case)	109.7 (72.3) 16.9 (19.8) 16.6 (15.5) 17.2 (16.9)	0.067 >0.05* >0.05* >0.05*

Abbreviations: NR, not reported; PVP, photoselective vaporisation of the prostate; RCT, randomised controlled trial

†Intervention (ejaculatory hood sparing GreenLight PVP) and comparator (standard GreenLight PVP) have been swapped in order to be consistent with reporting of other studies.
*Comparison between outcome measure at that time point compared to baseline/preoperative measure not a comparison between arms

Duration of catheterisation

Seven comparative studies reported on post-surgery catheterisation including: one RCT, four non-randomised comparative studies, two propensity matched cohorts. Four subgroup analyses also reported on this outcome, all of which were retrospective cohorts (three comparing anticoagulation status, one comparing between day-case and inpatient surgeries), Table 8.

Three studies reported a significantly shorter duration of catheterisation with GreenLight PVP than TURP. This included the propensity matched cohort by Cimino *et al.* (2017), 1.2 days for GreenLight PVP and 4.7 days for TURP, the non-randomised study by Mattevi *et al.* (2020) mean duration of 1.2 and 3.1 days for GreenLight PVP and TURP, and the non-randomised study by Reimann *et al.* (2019), median of 1 days for GreenLight PVP and 2 days for TURP. The latter also reported that removal of the suprapubic catheter was signficantly earlier in the GreenLight PVP arm; after median of 2 (range 2 to 3) days versus 3.5 (range 3 to 4) days, p<0.001. Mattevi *et al.* (2020) reported that transient recatheterisation was performed for urinary retention at catheter removal in 13 of 50 patients (26%) undergoing TURP, and in 3 of 50 patients (6%) undergoing GreenLight PVP.

No significant difference in duration of catheterisation between standard GreenLight PVP and ejaculatory hood sparing GreenLight PVP arms was observed in the RCT at 1, 3, 6 and 12 months follow-up (Abolazm *et al.* 2020). The non-randomised study by Hibon *et al.* (2017) reported a difference in duration of catheterisation between GreenLight PVP and anatomical PVP, mean 1.3 and 1.9 days respectively, however this would not have reached significance if accounting for multiple statistical testing. This study reported that post-operatively ten patients had acute urinary retention that required catheterisation.

Xu *et al.* (2021) reported a significant difference in duration of catheterisation between day-case and inpatient surgery patients; mean of 0.6 and 2.2 days respectively, p<0.01.

Lee *et al.* (2016) reported no difference in duration of catheterisation between patients taking anticoagulation (n=186) and those not (n=198), p=0.1. Knapp *et al.* (2017) reported a significant difference in duration of catheterisation between patients on anticoagulation (n=59, mean 1.35 days) and those not (no anticoagulation or aspirin, n=272, mean 0.65 days), but no difference between patients taking aspirin (n=42, mean 0.66 days) and those not (n=272). The study also reported that four patients taking anticoagulation and six patients taking neither anticoagulation nor aspirin required a 3-way irrigation catheter, however these were not statistically compared.

Goueli *et al.* (2017) reported a significant difference in duration of catheterisation between patients with (n=137) and without pre-operative urine retention (n=195), p<0.001. The study also reported that there was no statistical difference in the proportion of patients who failed the initial void trial between the retention and non-retention groups; 18.2% and 10.3% respectively, p=0.05. Meskawi *et al.* (2019) reported a significant difference in duration of catheterisation between patients based on anti-thrombotic therapy status (categorised as no antithrombotic, aspirin, other antiplatelet, anticoagulant), however it is unclear to the EAC if this would have remained significant if correction for multiple statistical testing had been applied. There was no significant difference in the need for long-term intermittent or permanent catheterisation across the subgroups: 4.0%, 3.4%, 4.2% and 2.7% respectively, p=0.9.

Table 8: Summary of comparative studies (N=11) reporting duration of catheterisation in days, reported as mean (SD), median [range] or median {IQR}

Author (year)	Study design (n)	Intervention	Duration, days	Comparator	Duration, days	p-value
Cimino *et al.* (2017)	Propensity matched cohort (n=110)	GreenLight PVP (n=55)	1.25 (0.98)	TURP (n=55)	4.67 (1.59)	<0.01
Castellani *et al.* (2018)	Propensity matched cohort (n=90)	GreenLight PVP (n=45)	2 [NR]	ThuVEP (n=45)	2 [NR]	0.120
Reimann *et al.* (2019)	Non-randomised (n=254)	GreenLight PVP (n=140)	1 {1 to 2}	TURP (n=114)	2 {2 to 3}	<0.001
Mattevi *et al.* (2020)	Non-randomised (n=100)	GreenLight PVP (n=50)	1.2 (0.5)	TURP (n=50)	3.1 (3.4)	<0.001
Cindolo *et al.* (2017)	Non-randomised (n=813)	GreenLight PVP (n=403)	1 [1 to 2]	GreenLight PVP (anatomical n=410)	1 [1 to 2]	0.082
Abolazm *et al.* (2020)†	RCT (n=49)	GreenLight PVP (n=24)	1 [1 to 5]	GreenLight PVP (ejac hood sparing, n=25)	1 [1 to 5]	0.49
Hibon *et al.* (2017)	Non-randomised (n=106)	GreenLight PVP (n=55)	1.3 (0.9)	Anatomical PVP (n=51)	1.9 (2.0)	0.046
Lee *et al.* (2016)	Cohort (n=384)	GreenLight PVP (no anticoag, n=198)	1 [1 to 2]	GreenLight PVP (anticoag, n=186)	1 [1 to 2]	0.1
Knapp *et al.* (2017)	Cohort (n=373)	GreenLight PVP (no anticoag or aspirin, n=272)	0.7 (0.8)	GreenLight PVP (anticoag, n=59)	1.4 (3.2)	0.002
				GreenLight PVP (aspirin, n=42)	0.7 (0.7)	0.930
Meskawi *et al.* (2019)	Cohort (n=322)	GreenLight PVP (no anti-thrombotic, n=274)	1 [1 to 1]	GreenLight PVP (aspirin, n=87)	1 [1 to 1]	<0.001
				GreenLight PVP (other antiplatelet, n=24)	1 [1 to 2]	
				GreenLight PVP (anticoag, n=37)	1 [1 to 2]	
Xu *et al.* (2021)	Cohort (n=312)	GreenLight PVP (inpatient, n=198)	2.2 (0.5)	GreenLight PVP (day-case, n=114)	0.6 (0.1)	<0.01

Abbreviations: PVP, photoselective vaporisation of the prostate; RCT, randomised controlled trial; TURP, transurethral resection of the prostate

†Intervention (ejaculatory hood sparing GreenLight PVP) and comparator (standard GreenLight PVP) have been swapped in order to be consistent with reporting of other studies.

Conducted exclusively in a patient cohort with retention, Gondran-Tellier *et al.* (2021) reported that post-operative success of catheter removal was achieved in 154 of 171 patients (90%) and was significantly different across TURP, PVP, endoscopic enucleation, PAE, open prostatectomy groups; 87.5%, 95.1%, 100%, 53.3%, 100% respectively, p<0.001. Urinary catheter-free rates without using BPH medications was similar between TURP and PVP at 12 months; 60.4% and 74.2%, p=0.15. Using backwards stepwise multivariate logistic regression analysis (adjusting for variables with p<0.20 in univariate analysis) with TURP as the reference, the following were significantly associated with failure to remove the catheter at 12 months: PVP (OR 0.27 [0.10 to 0.69], p=0.008), endoscopic enucleation (OR 0.08 [0.022 to 0.49], p=0.023), open prostatectomy (OR 0.10 [0.01 to 0.57], p=0.034), PAE (OR 5.27 [1.28 to 27.75], p=0.30), Charlson score (OR 1.36 [1.14 to 1.66], p=0.001), and number of preoperative trials without catheter failures (OR 2.53 [1.23 to 5.51], p=0.014).

The retrospective cohort by Meskawi *et al.* (2017) additionally reported that 10% of patients failed the first void trial after surgery; the majority (66%) occurring in men with indwelling catheter pre-operation.

The retrospective cohort analysis conducted by Campobasso *et al.* (2020) reported no difference in duration of catheterisation between patients with prostate volume less than 100 ml (n=916) and those with prostate volume greater or equal to 100 ml (n=115), p=0.769 undergoing GreenLight XPS PVP.

Rate of dysuria (pain)

The non-randomised comparative study by Mattevi *et al.* (2020) reported no significant difference in early dysuria or urge within 30 days of the PVP or TURP procedure, 32% (16 of 50) and 16% (8 of 50) respectively, p=0.06. Eken and Soyupak (2018) reported dysuria urgency in patients taking anticoagulation and those not as 5.1% and 6.9% respectively, the EAC has determined that there was no statistical difference using proportion test, p=0.85.

Quality of life measures

International Prostate Symptoms Score- Quality of Life (IPSS-QoL)

A total of four studies reported comparison of IPSS-QoL between arms, including one RCTs, and one propensity matched cohort, two retrospective cohorts (one comparing subgroups based on anticoagulation status, one comparing day-case and inpatient subgroups), Table 9.

The non-randomised study by Reimann *et al.* (2019) also reported the change in IPSS-QoL in GreenLight PVP and TURP arms, but at different time points (27 months and 36 months) respectively, therefore the EAC has excluded their statistical comparison.

No significant difference in IPSS-QoL between standard GreenLight PVP (intervention) and ejaculatory hood sparing GreenLight PVP (comparator) arms was observed at 1, 3, 6 and 12 months follow-up (Abolazm *et al.* 2020). Azizi *et al.* (2017) reported no significant difference in QoL scores between propensity matched GreenLight PVP and vaporincision arms at baseline and 6 month follow up.

Lee *et al.* (2016) reported an improvement in QoL at all follow-up timepoints up to 24 months, with no difference between patients taking anticoagulation and those not (other than at baseline).

Xu *et al.* (2021) reported significant improvements in IPSS-QoL up to 12 months follow-up when compared to baseline measurements, with no statistical comparison between day-case and inpatient patients.

Azizi *et al.* (2017) also reported a significant different in change in QoL from baseline and at 6 months within GreenLight PVP and vaporincision arms with a greater change noted with the latter intervention (-2.7 vs. -3.4, $p<0.001$). One additional study illustrated the change in quality of life but did not provide numerical values; Goueli *et al.* (2017) stratified a cohort by presence of pre-operative urine retention and reported a significant decrease in IPSS-QoL compared with baseline within each subgroup at all follow-up time points up to 24 months.

Table 9: Summary of comparative studies (N=4) reporting IPSS-QoL outcome; mean (SD), median [IQR]

Author (year)	Study design (n)	Timepoint	Intervention	IPSS-QoL, mean (SD)	Comparator	IPSS-QoL, mean (SD)	p-value
Abolazm *et al.* (2020)†	RCT (n=49)	Baseline 1 month 3 months 6 months 12 months	GreenLight PVP	5.3 (0.68) NR NR NR NR	GreenLight PVP (ejac hood sparing)	5.6 (0.58) NR NR NR NR	0.07 0.6 0.5 0.5 0.07
Azizi *et al.* (2017)	Propensity matched (n=444)	Baseline 6 months	GreenLight PVP	4.1 1.3	GreenLight vaporincision	4.3 1.1	0.33 0.57
Lee *et al.* (2016)	Cohort (n=384)	Baseline 1 month 3 months 6 months 12 months 2 years	GreenLight PVP (no anticoag)	4 [3 to 5] 2 [1 to 4] 1 [1 to 3] 1 [1 to 2] 1 [1 to 3] 2 [1 to 3]	GreenLight PVP (anticoag)	3 [3 to 5] 2 [1 to 3] 1 [1 to 2] 1 [1 to 2] 0 [1 to 2] 2 [1 to 3]	<0.01 0.74 0.47 0.41 0.18 0.91
Xu *et al.* (2021)	Cohort (n=312)	Baseline 3 months 6 months 12 months	GreenLight PVP (inpatient)	4.4 (0.8) 2.3 (0.7) 2.2 (0.8) 2.2 (0.7)	GreenLight PVP (day-case)	4.6 (0.9) 2.4 (0.8) 2.2 (0.7) 2.1 (0.7)	0.061

Abbreviations: IPSS-QoL, international prostate score quality of life; RCT, randomised controlled trial; PVP, photoselective vaporisation; QoL, quality of life

†Intervention (ejaculatory hood sparing GreenLight PVP) and comparator (standard GreenLight PVP) have been swapped in order to be consistent with reporting of other studies.

Patient Global Impression of Improvement (PGI-I)

Three studies reported on the Patient Global Impression of Improvement (PGI-I). Castellani *et al.* (2018) reported no difference in perception of improvement between GreenLight or ThuVEP arms at six months, p=0.306. Cindolo *et al.* (2017) reported no difference in outcomes between GreenLight PVP and anatomical PVP arms, p=0.420; however the time of this measurement was not explicitly defined. Campobasso *et al.* (2020) reported that there was a difference in PGI-I between patients with prostate volume smaller than 100 ml and those not, as determined by chi-squared test across all seven categories, p=0.012, however the timepoint of the questionnaire was poorly reported, Table 10.

Table 10: Summary of studies (N=1) reporting on Patient Global Impression of Improvement (PGI-I), mean (IQR)

PGI-I	Prostate volume <100 cc (n=916)	Prostate volume ≥100 cc (n=115)
1	447 (48.8)	63 (54.8)
2	272 (29.7)	30 (26.1)
3	68 (7.4)	2 (1.7)
4	22 (2.4)	2 (1.7)
5	8 (0.9)	0 (0)
6	3 (0.3)	1 (0.9)
7	0 (0)	1 (0.9)

Preservation of sexual function

Only one RCT was specifically powered to detect a significant difference in antegrade ejaculation. Abolazm *et al.* (2020) reported a significant difference in the proportion of patients with antegrade ejaculation, 85% and 31.6%, between patients undergoing ejaculatory hood sparing GreenLight PVP and standard GreenLight PVP respectively, p=0.001.

Sexual function and health was measured using a variety of patient questionnaires across the included studies.

Ejaculatory Domain of Male Sexual Health Questionnaire (EjD-MSHQ)

The propensity matched cohort by Cimino *et al.* (2017) reported significantly higher ejaculatory function (defined as EjD-MSHQ>0) at 12 months with GreenLight PVP than TURP, 34.5% and 58.8% respectively, p=0.007.

The RCT by Abolazm *et al.* (2020) reported a significant reduction in the EjD-MSHQ score after standard GreenLight PVP at 6 and 12 months (each p<0.001 when compared with baseline), and no significant difference after ejaculatory hood sparing GreenLight PVP (p=0.18 and 0.078, respectively). The median EjD-MSHQ score was higher for ejaculatory hood sparing technique; 28.5 (range 1 to 33) and 27 (range 1 to 33) at 6 and 12 months, when compared with standard GreenLight PVP; 9.5 (range 1 to 35) and 9 (range 0 to 33) at 6 (p=0.005) and 12 months (p<0.001).

International Index of Erectile Function-15 (IIEF-15)

Abolazm *et al.* (2020) reported a significant reduction in IIEF-15 score at 1 year with standard GreenLight PVP (mean 58.4 at baseline, median 48 at 12 months post-operation; p<0.001), but not with ejaculatory hood sparing GreenLight PVP (mean 58.8 at baseline, median 53.5 at 12 months; p=0.18).

Sexual Health Inventory for Men (SHIM)

The propensity matched cohort reported by Cimino *et al.* (2017) found no significant difference in SHIM between TURP and GreenLight PVP at 3, 6 and 12 months.

Length of hospital stay

Eight comparative studies reported on hospital length of stay, including one RCT, six non-randomised comparative studies and one propensity matched cohort. Three retrospective cohort studies also reported on this outcome (all comparing subgroups based on anticoagulant/antiplatelet status), Table 11.

Reimann *et al.* (2019) reported a significant difference in length of stay of GreenLight PVP when compared to TURP; median of two and four days respectively, p<0.001. Prolonged hospital stays (greater than 2 days for GreenLight PVP and four days for TURP) were more common in in the TURP arm; 37% and 58% respectively, p=0.001. Gondran-Tellier *et al.* (2021)

reported a significant difference in length of stay between TURP, PVP, endoscopic enucleation, prostate artery embolisation and open prostatectomy in a cohort of patients undergoing surgery exclusively with retention. They reported that length of stay was shorter in the PVP arm compared with TURP; medians of 5 days and 6 days respectively, p=0.002. The non-randomised study by Mesnard *et al.* (2021) conducted exclusively in patients with haemophilia reported longer hospital length of stay in TURP versus GreenLight PVP, medians nine and five days respectively; however no statistical comparison was conducted due to small sample size (n=10). Castellani *et al.* (2018) found no difference in length of stay between propensity matched patients undergoing GreenLight PVP and those undergoing ThuVEP, p=0.088.

Cindolo *et al.* (2017) reported no difference in hospital stay between GreenLight PVP and anatomical PVP, p=0.25. Abolazm *et al.* (2020) reported no significant difference in hospital stay between standard GreenLight PVP and ejaculatory hood sparing GreenLight PVP. The non-randomised study by Hibon *et al.* (2017) similarly reported no significant difference in length of hospital stay between GreenLight PVP and anatomical PVP.

Knapp *et al.* (2017) reported a significant difference in duration of hospital stay between patients on anticoagulation and those not (no anticoagulation or aspirin), but no difference between patients taking aspirin and those not. Goueli *et al.* (2017) reported that patients with preoperative urine retention experienced longer hospital stay (p=0.002). Meskawi *et al.* (2019) reported a significant difference in length of hospital stay between patients based on anti-thrombotic therapy status (categorised as no antithrombotic, aspirin, other antiplatelets, anticoagulant), however it is unclear to the EAC if this would have remained significant if correction for multiple statistical testing had been applied. The retrospective cohort analysis conducted by Campobasso *et al.* (2020) reported a median (IQR) length of post-operative stay as 2 (1 to 2) days, with no difference between patients with prostate volume less than 100 ml (n=916) and those with prostate volume greater or equal to 100 ml (n=115), p=0.126.

Table 11: Summary of comparative studies (N=11) reporting on length of stay (LoS) in days, reported as mean (SD), median [IQR] or median {range}

Author (year)	Study design	Arm 1	LoS, days	Arm 2	Comparator	p-value
Reimann *et al.* (2019)	Non-randomised (n=254)	GreenLight PVP (n-140)	2 {2 to 4}	TURP (n=114)	4 {3 to 5}	<0.001
Mathieu *et al.* (2017)	Non-randomised (n=214)	GreenLight PVP (n=51)	2.8 (2.9)	TURP (monopolar, n=99)	3.4 (2.3)	<0.001
				Open prostatectomy (n=23)	8.0 (3.8)	
				HoLEP/ThuLEP (n=64)	2.6 (2.5)	
Gondran-Tellier *et al.* (2021)	Non-randomised (n=171)	GreenLight PVP (n=62)	5 [5 to 6]	TURP (mono- and bi-polar, n=48)	6 [5 to 7]	<0.001
				Endoscopic enucleation (n=21)	3 [3 to 3]	
				PAE (n=15)	3 [3 to 4]	
				Open prostatectomy (n=25)	11 [10 to 12]	
Mattevi *et al.* (2020)	Non-randomised (n=100)	GreenLight PVP (n=50)	1.7 (0.8)	TURP (n=50)	3.8 (2.6)	0.001
Castellani *et al.* (2018)	Propensity matched (n=90)	GreenLight PVP (n=45)	2 [NR]	ThuVEP (n=45)	3 [NR]	0.088
Cindolo *et al.* (2017)	Non-randomised (n=813)	GreenLight PVP (n=403)	2 [1 to 3]	GreenLight PVP anatomical (n=410)	2 [1 to 2]	0.25
Abolazm *et al.* (2020)†	RCT (n=49)	GreenLight PVP (n=24)	1 [1 to 3]	GreenLight PVP (ejac hood sparing, n=25)	1 [1 to 2]	0.64
Hibon *et al.* (2017)	Non-randomised (n=107)	GreenLight PVP (n=55)	2.0 (1.6)	Anatomical PVP (n=51)	2.5 (1.6)	0.111
Lee *et al.* (2016)	Cohort (n=384)	GreenLight PVP (no anticoagulation, n=198)	3.5 [1 to 4]	GreenLight PVP (anticoagulation, n=186)	4 [1 to 4]	<0.01
Knapp *et al.* (2017)	Cohort (n=373)	GreenLight PVP (no anticoag or aspirin, n=272)	1.0 (0.7)	GreenLight PVP (anticoag, n=59)	1.9 (3.4)	<0.001
				GreenLight PVP (aspirin, n=42)	1.0 (0.6)	0.992
Meskawi *et al.* (2019)	Cohort (n=322)	GreenLight PVP (no antithrombotic, n=274)	0 [0 to 1]	GreenLight PVP (aspirin, n=87)	1 [0 to 1]	<0.001
				GreenLight PVP (other antiplatelet, n=24)	1.5 [1 to 3]	
				GreenLight PVP (anticoag, n=37)	1 [0 to 2]	

Abbreviations: NR, not reported; PAE, prostate artery embolization; PVP, photoselective vaporisation of the prostate; RCT, randomised controlled trial; TURP, transurethral resection of the prostate; ThuVEP, thulium laser vaporesection of the prostate
†Intervention (ejaculatory hood sparing GreenLight PVP) and comparator (standard GreenLight PVP) have been swapped in order to be consistent with reporting of other studies.

Frequency of completion as day-case

Four studies explicitly reported the proportion of patients undergoing GreenLight intervention as a day-case procedure, ranging between 36.5% and 90.3%, Table 12.

Table 12: Summary of studies (N=4) reporting on day-case procedure rates.

Author (year)	Proportion of procedures conducted as day-case
Berquet *et al.* (2015)	121/134 (90.3%)
Trail *et al.* (2021)	366/538 (68.0%)
Xu *et al.* (2021)	114/312 (36.5%)
Zhou *et al.* (2017)	234/327 (71.6%)
†Calculated by EAC	

The cohort study by Berquet *et al.* (2015) reported that 90.3% of GreenLight PVP procedures were conducted as a day-case procedure, and that reasons for hospital overnight stay for 9 of 13 procedures were due to organisational or logistical reasons. The UK study by Trail *et al.* (2021) reported that 68% (366 of 538) were managed as day-cases, but that 96% (519 of 538) were discharged within 23 hours of admission.

The retrospective cohort by Trail *et al.* (2021) reported subgroup analysis and compared results of day-cases (n=366) and and those with overnight stay (n=172). The authors report that patients undergoing intra-operative conversion to TURP were more likely to remain in hospital overnight (1.1% versus 7.1% in day-case and those with overnight stay respectively, OR 6.44 [2.02 to 20.57], p=0.002). The study also reported that patient-reported satisfaction was higher (89.6% versus 81.6%, p=0.03) and reoperation rate lower (5.7% versus 10.5%), p=0.04) in day-case patients compared to those who remained in hospital overnight. In univariate analysis, age of 80 year or older, ASA score of 3 or greater, prostate volume of 80 ml and operation time of 60 minutes or greater were all significant predictors of overnight stay following GreenLight PVP procedure. In multi-variate analysis, age of 80 years or greater and ASA score of 3 or greater remained predictors of overnight stay.

An additional retrospective cohort study by Xu *et al.* (2021) included 312 patients undergoing GreenLight PVP during a study period, of which 114 (37%) were indicated for day-case surgery. However, the author reported that 4 of 114 (3.5%) had delayed discharge beyond 24 hours due to high fever in 1 patient, and gross haematuria requiring bladder irrigation in 3 patients.

Rate of readmission

The EAC has interpreted this outcome to also include retreatment. The EAC have not tabulated this outcome due to the variation in time points reported and inconsistent reporting of reinterventions and readmission types.

The non-randomised study by Reimann *et al.* (2019) reported that post-operative re-intervention due to bleeding (Clavien-Dindo >IIIa) was required in 3 of 114 TURP patients (12%), and in none of the 140 patients receiving GreenLight PVP, however the difference was not statistically significant, p=0.09. Overall need for re-intervention was the same between GreenLight PVP and TURP arms; 4% and 10%, p=0.09 although time points were not reported. The non-randomised study by Gondran-Tellier *et al.* (2021) reported that 26 of 171 patients (15.2%) had recurrence of acute urinary retention, and 5 (2.9%) required reoperation within 12 months of the original procedure; 3 after PAE, 1 after TURP, 1 after PVP, and 0 after open prostatectomy or endoscopic enucleation, p=0.01. The non-randomised study by Mattevi *et al.* (2020) reported that five patients in the TURP arm, experienced bladder neck sclerosis or prostate tissue regrowth requiring additional TURP surgery within one year. None of the patients in the GreenLight PVP arm required additional intervention, p=0.02. Castellani *et al.* (2018) reported that reoperation after 30 days was not significantly different between propensity matched GreenLight PVP and ThuVEP patients; 6.7% and 8.9%, p=0.694.

The propensity matched study by Azizi *et al.* (2017) reported that post-operative visits to the emergency department and hospitalisations for complications were not significantly different between GreenLight PVP and GreenLight vaporincision arms. However, in the early post-operative period (within 90 days), more clinic visits were observed in the GreenLight PVP arm; 14.4% versus 5.9%, p=0.004.

Abolazm *et al.* (2020) reported that 7 of the 46 patients (15.2%) followed to 1 year required retreatment; 3 in standard GreenLight PVP and 4 in the ejaculatory hood sparing GreenLight PVP, p=0.4. Reasons for repeat procedure included three residual adenoma, three incisions for bladder neck contracture and one resection loop clearance of heavy prostatic fossa encrustation. Cindolo *et al.* (2017) reported that a second intervention was required in 3.1% of patients; 16 patients in the GreenLight PVP arm and 8 in the anatomical PVP arm, however no statistical comparison was conducted and no time period defined. Only one patient in standard GreenLight PVP arm required an implant of a prosthesis for urinary incontinence.

Mathieu *et al.* (2017) reported that 26 of 237 (11%) required readmission, however did not report readmission by the type of original procedure (monopolar TURP, open prostatectomy, HoLEP, ThuLEP, or PVP) and did not describe the duration of follow-up. The study reported that prostate volume and ASA score were independent predictors of overall complications (p=0.01 and p=0.02 respectively) while technique was not (p=0.71).

The study by Mesnard *et al.* (2021), conducted exclusively in patients with haemophilia, reported that three patients presented with complications with two requiring readmission after hospital discharge following GreenLight PVP. Patients with haemophilia A had abnormal haematuria and one required surgical revision. In a cohort exclusively at high risk of bleeding, Waters *et al.* (2021) reported that 22 of 374 (5.9%) patients required readmission: 12 due to urinary retention (requiring temporary urethral catheterisation, with prostate volume being greater than 100 ml in 5 patients) and 10 due to haematuria (prostate volume being greater than 100 ml in 9 patients, 8 managed with urethral catheter and continuous bladder irrigation until urine cleared, 2 required cystoscopy and bladder washout). Eken and Soyupak (2018) reported the need for reoperation within 3 months was 1.7% (1 of 59) in patients taking anticoagulation and 2.3% (4 of 174) in patients not on anticoagulation, with no significant difference in proportions determined by the EAC.

The database by Campobasso *et al.* (2020) reported that 25 of 1,031 (2.4%) required reintervention including 11 TURP (1.0%), 8 bladder neck incision (0.8%), 6 urethrotomy (0.6%). The retrospective database by Law *et al.* (2021) reported that 13.2% required readmission within 30 days with the majority being visits to the emergency department for grade I haematuria. In 569 patients followed up to 60 months, BPH recurrence requiring surgical reintervention was reported in 10 patients (1.5%) within 60 months, and 19 patients (3.3%) were restarted on BPH medications. Berquet *et al.* (2015) reported that 2 of 134 (1.5%) were rehospitalised within the first month post-operatively, both were readmitted for haematuria requiring bladder irrigation.

Meskawi *et al.* (2017) reported that complications requiring intervention under regional or general anaesthesia (Clavien-Dindo III) were recorded in 3.9% of patients. Retreatment rates were 0.9% within 0 to 12 months, 5.4% within 12 to 24 months, 9.3% within 24 and 36 months, and 2.4% within 36 to 48 months. The study reported that retreated patients were more likely to have larger prostate volume; 150 ml versus 120 ml, p=0.002.

Meskawi *et al.* (2019) reported that 30-day readmission rates were significantly different depending on patients' medical therapy use: those taking no anti-thrombotics (4%), aspirin (8%), other antiplatelets (12.5%), and anticoagulants (16.2%), p=0.02. Retreatment rates were not significantly different across groups: 1.5%, 0%, 4.2%, and 0% respectively, p=0.3.

Lee *et al.* (2016) reported that there was no difference in the number of patients requiring reoperation between anticoagulation and no anticoagulation subgroups; four patients and three patients respectively (p=0.49), six of which were due to refractory haematuria, and one post-operative urethral stricture. The study also reported that there were no differences in readmissions across arms, and that the number of anticoagulant the patient was taking was not associated with reoperation outcome.

Goueli *et al.* (2017) reported that PVP failure (defined as chronic retention requiring chronic Foley or clean intermittent catheterisation (CIC) was not significantly different between patients with preoperative urine retention and

those without; 5.8% and 2.1% respectively, p=0.1. The study also reported that the need for BPH retreatment within 24 months was not statistically different between arms; 3 patients with pre-operative retention, 0 patients without, p=0.1. The authors found no difference in age, history of diabetes, history of neurological disease, prostate volume, catheterisation type, PVR, or duration of pre-operative catheterisation between patients with failed PVP (requiring permanent or intermittent catheterisation) and those who did not.

Procedural blood loss and blood transfusion requirement

The need for blood transfusion in patients receiving GreenLight therapy was reported in 12 studies; 10 intra-operatively (between 0% and 2.2%) and 2 within 30 days post-operatively (0.6% and 0.8%), Table 13.

Table 13: Summary of studies (N=12) reporting on blood transfusion following GreenLight PVP.

Author (year)	Timepoint	Blood transfusion
Mattevi *et al.* (2020)	Intra-operatively and post-operatively combined	GreenLight PVP: 0/50 (0%) TURP: 4/50 (8%)
Mesnard *et al.* (2021)	Intra-operatively	GreenLight PVP: 0/5 (0%) TURP: 0/5 (0%)
	Post-operatively	GreenLight PVP: 0/5 (0%) TURP: 0/5 (0%)
Castellani *et al.* (2018)	Intra-operatively	GreenLight PVP: 1/45 (2.2%) ThuVEP: 1/45 (2.2%)
Meskawi *et al.* (2019)	Intra-operatively	2/422 (0.5%) - no antithrombotic: 0/274 - aspirin: 1/87 - other antiplatelets: 1/24 - anticoagulant: 0/37
Goueli *et al.* (2017)	Intra-operatively	Retention: 2/137 (1.5%) No retention: 0/198 (0%)
Hibon *et al.* (2017)	Intra-operatively	1/106 (0.9%)
Lee *et al.* (2016)	Intra-operatively	0/384 (0%)
Knapp *et al.* (2017)	Intra-operatively	0/373 (0%)
Xu *et al.* (2021)	Intra-operatively	0/312 (0%)
Eken and Soyupak (2018)	Intra-operatively	0/233 (0%)
Campobasso *et al.* (2020)	30 days	6/1031 (0.6%) - Prostate volume <100ml: 6/916 - Prostate volume ≥100ml: 0/115
Cindolo *et al.* (2017)	30 days	6/813 (0.7%) - Standard PVP: 3/403 (0.8%) - Anatomical PVP: 3/410 (0.8%)
Abbreviations: PVP, photoselective vaporisation of the prostate; ThuVEP, thulium vapoenucleation of the prostate; TURP, transurethral resection of the prostate		

The non-randomised comparative study by Mattevi *et al.* (2020) reported a significant difference in haemoglobin reduction between GreenLight PVP and TURP; 0.46 and 1.8 g/L, p=0.01. In this study four patients in the TURP arm and none in the GreenLight PVP arm required a blood transfusion, p=0.04. Conducted exclusively in a cohort of patients with haemophilia, Mesnard *et al.* (2021) reported that blood loss was higher in the TURP group (n=5) with a median haemoglobin decrease of 20 g/L compared with 14 g/L in the GreenLight PVP group (n=5); however statistical comparison was not conducted due to small sample size.

Meskawi *et al.* (2019) reported that the median drop in haemoglobin was not significantly different across subgroups; no anti-thrombotic (7 g/dl), aspirin (8 g/dl), other antiplatelets (8 g/dl), anticoagulation (6 g/dl), p=0.8. Two patients with baseline haemoglobin value of 80 g/dl required blood transfusion after surgery. Serious bleeding events were present in 16.8%, 16.1%, 16.7%, and 10.8% of patients across the respective subgroups. Multi-variate analysis found that none of the subgroups of patients were at higher risk of serious bleeding events when compared to patients taking no anti-thrombotic medication when adjusting for age, prostate volume, retention status, comorbidity score and 5ARI use.

Reimann *et al.* (2019) reported that intraoperative bleeding with the need for extensive coagulation as the most common adverse event was significantly lower in the PVP group than TURP, 5% and 14% respectively, p<0.01.

Eken and Soyupak (2018) reported 10 of 233 patients (4.3%) experienced bleeding, but that there was no difference in the incidence of bleeding between the anticoagulation and non-anticoagulation groups; 5.1% and 4.0%, p-value not reported.

Rate of transurethral resection syndrome (TUR)

TUR syndrome is caused by the absorption of electrolyte-free irrigating fluid (Hahn 1991). GreenLight XPS IFU advise on the use of saline fluid for irrigation. The use of saline fluid for irrigation reduces the risk of TUR and hyponatremia due to the presence of electrolytes in the fluid although excess

fluid absorption can still be experienced (Wettstein *et al.* 2016; Hahn 2006; Porsch *et al.* 2016).

TUR syndrome was explicitly recorded as an outcome measure in 5 studies, but only occurred in 1 patient across a total of 1,004 (0.1%) patients reported, Table 14. The authors did not specify the type of irrigation fluid used where the patient experienced TUR syndrome (Reimann *et al.* 2018).

Table 14: Summary of studies (N=5) which reported on Transurethral Resection syndrome (TUR)

Author (year)	TUR
Reimann *et al.* (2018)	1/375 (0.3%)
Xu *et al.* (2021)	0/312 (0%)
Liu *et al.* (2020)	0/150 (0%)
Tao *et al.* (2019)	0/102 (0%)
Chen and Chiang (2016)	0/65 (0%)
Abbreviations: TUR, transurethral resection syndrome	

One study, identified during the EAC literature search, reported on the irrigation fluid absorption in patients undergoing GreenLight PVP and bipolar TURP (Porsch *et al.* 2016). A significantly higher level of fluid absorption was detected in patients undergoing TURP compared with GreenLight PVP with 25 of 35 (71%) and 14 of 26 (54%) patients respectively, p=0.006. The absorption of irrigation fluid is possible during any transurethral surgery and the risks associated depend on the type of fluid used is not considered to be a risk or adverse event exclusive to GreenLight PVP.

Rate of capsular perforation

Capsular perforation was recorded as an outcome measure in 17 studies; 6 of which reported no capsular perforations, the proportion of patients experiencing capsular perforation in the 11 remaining studies ranged between 0.1% and 5.6%, Table 15.

Table 15. Summary of studies (N=17) reporting on capsular perforation.

Author (year)	Country	Capsular perforation
Gasmi *et al.* (2021)	France, Spain	83/1,491 (5.6%)
Meskawi *et al.* (2017)	Canada, France, USA	12/438 (2.7%)
Law *at al.* (2021)	Canada, France, Germany, Italy, Mexico, Brazil and Argentina	21/1,471 (1.4%)
Castellucci *et al.* (2020)	Italy	6/487 (1.2%)
Zhou *et al.* (2017)	Canada	4/328 (1.2%)
Knapp *et al.* (2017)	Australia	3/373 (0.8%)
Campobasso *et al.* (2020)	Italy	8/1,031 (0.8%)*
Cindolo *et al.* (2017)	Italy	5/813 (0.6%)
Liu *et al.* (2020)	China	1/150 (0.7%)
Azizi *et al.* (2017)	Canada, USA	1/444 (0.2%)†
Rajih *et al.* (2017)	Canada, USA	1/941 (0.1%)
Xu *et al.* (2021)	China	0/312 (0%)
Ghahhari *et al.* (2021)	Italy	0/193 (0%)
Ghahhari *et al.* (2018)	Italy	0/140 (0%)
Tao *et al.* (2019)	China	0/102 (0%)
Aboutaleb *et al.* (2018)	Egypt, United Arab Emirates	0/75 (0%)
Thomas *et al.* (2019)	Canada, USA	0/58 (0%)

†occurring in GreenLight vaporincision technique
*all occurring in patients with prostate volume less than 100 ml.

Device related adverse events

The majority of the included studies reported on adverse events (55 of 56; 98%), however the EAC considered only three that reported specifically on device-related events occurring intraoperatively. The retrospective cohort by Trujillo *et al.* (2021) reported 3 of 587 (0.5%) experienced conversion to TURP due to technical failures with the GreenLight XPS laser (fibre fracture and fibre failure). The retrospective cohort by Rajih *et al.* (2017) reported malfunction of the GreenLight XPS MoXy fibre (metal to glass cap detachment) in 3 of 941 patients (0.3%). Ferrari *et al.* (2021b) analysed surgical smoke from five patients and irrigation fluid from five different patients, all undergoing GreenLight PVP procedures for BPH. The study reported that 4 organic and potentially toxic compounds were found within the smoke samples, and up to 16 in the outflow irrigation fluid.

6 Adverse events

Safety outcomes identified from the clinical evidence has been summarised in Section 5. The majority of studies (55 of 56) identified by the EAC recorded

adverse events as an outcome measure. However, the EAC has focused on comparative studies, and those comparing risk groups in this narrative review.

The non-randomised study by Reimann *et al.* (2019) reported that there was no significant difference in overall adverse events including long-term complications between PVP and TURP; 53% and 90% respectively, p=0.28. Post-operative acute urine retention was the most common complication, and was not significantly different across GreenLight and TURP arms; 6% and 10%, p=0.24. Post-operative urge incontinence was also comparable across groups; 2% and 3% respectively, p=0.80. The non-randomised study by Gondran-Tellier *et al.* (2021) reported a significant difference in 30-day post-operative complications across TURP, PVP, endoscopic enucleation, PAE and open prostatectomy; 27%, 19%, 24%, 33% and 64% respectively, p=0.002. Clavien-Dindo grade I and II complications were highest in PAE and open prostatectomy arms, p=0.046, and grades 3 and above only occurred in TURP and open prostatectomy arms, p=0.027. However, the EAC notes that the number of patients in each arm were small, and that the study would not have been powered to detect these small differences. The non-randomised study by Mattevi *et al.* (2020) reported no significant difference in minor complications (based on the Clavien-Dindo classification) between patients undergoing GreenLight PVP or TURP. However, a difference in major complications was observed between arms: 7 of 50 (14%) in TURP arm and none in the GreenLight PVP arm, p=0.01. The non-randomised study by Mesnard *et al.* (2021) conducted exclusively in patients with haemophilia, reported that no intraoperative complications occurred in patients undergoing TURP (n=5) and those undergoing GreenLight PVP (n=5).

The non-randomised study by Hibon *et al.* (2017) reported 10 (18.2%) conversions to TURP in the GreenLight PVP arm, and none in the anatomical vaporisation arm. No difference in overall total of complications, minor (Clavien-Dindo categories I and II) or major (categories III and IV), however length of follow-up was significantly different between arms. Three cases of bladder-neck sclerosis and four cases of retromeatal stenosis required an urethrotomy (two in each arm). Minor complications included: 11 urinary

infections, 9 irritative symptoms. Major complications included surgery for clot removal and haemostasis; two in GreenLight PVP and three in anatomical PVP arms. Abolazm *et al.* 2020 (RCT; n=49) reported complications occurring intraoperatively or within the first 30 days: 2 cases of pyrexia, 1 failed first voiding trial, 1 post-operative retention, 3 epididymo-orchitis, 1 post-operative haematuria. The propensity matched retrospective cohort by Azizi *et al.* (2017) reported that there were no difference in intraoperative or post-operative Clavien-Dindo grade I adverse events between vaporincision and PVP arms. However, a difference in Clavien-Dindo grade II complications was found; 47 in the PVP arm and 21 in the vaporincision arm (Azizi *et al.* 2017).

Meskawi *et al.* (2019) reported no difference in overall 30-day complication rates between 4 subgroups of patients based on preoperative medical therapy: no anti-thrombotics (31%), aspirin (28.7%), other antiplatelets (45.8%), and anticoagulants (45.9%), p=0.4. Haematuria Clavien-Dindo I complications within 30 days were significantly different across subgroups: no anti-thrombotics (8.4%), aspirin (9.2%), other antiplatelets (25%), and anticoagulants (27%), p<0.001. Only one patient required a surgical intervention to stop the bleeding postoperatively, p=0.02.

Lee *et al.* (2016) reported that 48 of 384 (12.5%) patients experienced a complication; 27 in 30 days, 11 within 90 days, and no significant difference in number or timing of complications between patients taking anticoagulation (n=186) and those not (n=198). The study reported that there was a significantly higher rate of conversion to TURP in patients on anticoagulation; 13.5% versus 6.1%, p=0.01; however as anticoagulation is associated with a comorbidity, it is not possible to directly attribute causation to GreenLight therapy.

Knapp *et al.* (2017) reported an overall complication occurring in 22% of patients (82 of 373), occurring in 18 patients taking anticoagulation, 10 aspirin and 54 taking neither. The majority of complications (79%) were low grade (Clavien-Dindo I or II), with the most frequent being recatheterisation in 13 patients, acute urinary retention in 12, UTI in 8, haematuria in 6. No patient deaths were recorded within 90 days. One patient taking anticoagulation

developed sepsis and atrial fibrillation requiring cardioversion. The study reported no statistical difference in overall complication rates between patients taking anticoagulation and those not taking anticoagulation or aspirin (p=0.07). However, a significant difference in the number of patients experiencing a high-grade complications and a significant difference in patients not experiencing any complications between patients on anticoagulation (n=59) and those not taking anticoagulation or aspirin (n=314) was reported (p=0.011). The study also reported intraoperative adverse events by type of anticoagulation: 9 of 23 on warfarin, 0 of 4 heparin, 6 of 20 clopidogrel, 2 of 9 new oral anticoagulant (NOAC), however the EAC notes that the study was not powered to detect differences in this outcome.

Goueli *et al.* (2017) reported no difference in the proportion of patients requiring conversion to TURP between patients with pre-operative retention (n=137) and those not (n=195); 3.6% and 2.6% respectively, p=0.5. The study found no significant difference in overall complications at 30 days between patients with and without pre-operative urine retention; 29.2% versus 35.9%, p=0.3. However a significant difference in 90-day complications was observed between groups; 21.2% in patients with retention, and 35.4% in those without, p=0.02, with non-retention patients having significantly more LUTS Clavien-Dindo II complications requiring medical intervention. The study reported no Clavien-Dindo grade III complications in either group across the median follow-up of 24 months.

Xu *et al.* (2021) reported no intraoperative complications in their retrospective cohort study of 312 patients undergoing GreenLight PVP surgery. The most common post-operative complications were urinary tract infection (UTI) and urinary retention. No significant difference in the proportion of patients experiencing UTI was observed between day-case and inpatient subgroups. Transient urinary retention requiring re-catheterisation was higher in the day-case subgroup; 14 of 114 (12.3%) versus 11 of 198 (5.6%), p<0.05, however the authors report that all cases had indwelling catheters, and these were successfully removed after 3 to 5 days. Irritative symptoms and urge urinary incontinence were the most common Clavien-Dindo grade I and II

complications, however there were no significant differences between subgroups.

The retrospective cohort analysis conducted by Campobasso *et al.* (2020) reported early complications in 385 of 1,031 patients (37.3%), with the most frequent complication being burning urination (13.2%). In subgroup analysis, patients with a large prostate volume (greater or equal to 100 ml) were at greater risk of developing an early complication in univariate and multivariate analysis (when adjusting for age, baseline PSA, BPH or LUTS therapy, antiplatelet or anticoagulation therapy, surgery type (standard or anatomical) and history of indwelling catheter prior to surgery); OR 1.8 [95%CI 1.2 to 2.9], p=0.009. Late complications were reported in 142 of 1031 patients (13.8%), with the most common late complication being storage symptoms with *de novo* urgency (4.8%). Patients with a large prostate volume were also at increased risk of developing a late complication in univariate and multi-variate analysis; OR 2.2 [95%CI 1.3 to 3.9], p=0.004.

One paper identified from the EAC literature search summarised 2,567 MAUDE (FDA) reports relating to the surgical treatment of BPH (TURP, HoLEP, GreenLight and UroLift) between January 2015 to October 2017 (Patel *et al.* 2019). 90.2% of reports identified related to GreenLight (n=2,315) with all but 0.1% (requiring minor intervention or classed as moderate complication, n=2) classed as mild complications. Overall, 68.8% (n=1,592) were reports of tip fracture or detachment; 29.4% (n=681) end firing; 1.2% (n=27) fibre body breakage; 0.6% (n=15) failure to fire. Two extraperitoneal bladder perforations were reported with GreenLight related to misuse by the user. 99.3% of all device complications were found to have no significant patient-related harm or complications.

The EAC searched the MAUDE (FDA) database on 03/12/2021 using the search terms ‘GreenLight’; ‘MoXy’; ‘GreenLight XPS’, ‘Boston Scientific’ and identified 500 adverse event reports between 01/01/2021 (from the guidance review report) and 30/11/2021. GreenLight XPS had 32 and MoXy Fibers had 468 associated adverse events during these dates respectively. Common issues relating to MoXy Fibers included: fibre tip and cap damage, including

breakage and detachment; forward firing; loss of power; fibre burnout. Most adverse events were resolved through the replacement of the fibre during the procedure with five reports (1%) of low severity injuries or affects: hematuria (n=1), urinary retention (n=3), user burn (n=1).

The 32 adverse events relating to the GreenLight XPS Laser console were as follows:

- Error codes and faults including screen failures, inability to switch on, test failure, not reaching power, hygiene errors (n=17)
- Foot pedal related issues including sticking, rust or corrosion, failure, detachment, locking, general error (n=8)
- Machine defects including smoke, burning smell, water leak and overheating (n=7)

In 17 cases it was explicitly reported that the patient were under general anesthesia at the time the procedure was cancelled; anaesthesia status unreported in remaining 15 cases. In one case the procedure was converted to TURP. No adverse event reported patient harm. The report outcomes and events identified by the EAC were consistent to those from Patel *et al.* (2021).

The EAC identified one MHRA field safety notice issued 06/04/2020 relating to the likelihood of metal cap and fibre tip break temperature related complaints. The Company initiated a Product Advisory response for the GreenLight MoXy Laser Fibers reinforcing existing instructions within the Instructions for Use (IFU) and updated guidance to increase irrigation flow to increase the liquid cooling effect to reduce temperature related complaints.

7 Evidence synthesis and meta-analysis

Ten systematic reviews were identified in the EAC literature search. However due to heterogeneity in the population (different risk factors, different severity and duration of symptoms), intervention (mixture of GreenLight XPS and HPS consoles, different power settings (80 W, 120 W, 180 W), different fibres,

different surgical techniques), comparator, and eligibility criteria across studies, the EAC does not consider the outcome of these systematic reviews and meta-analysis in line with the NICE Final Scope.

Through its independent literature search, the EAC only identified one randomised controlled trial (Abolazm *et al.* 2020). This RCT was powered to detect difference in persevered antegrade ejaculation between two surgical techniques both using GreenLight PVP (including ejaculatory hood sparing technique). Therefore, the EAC considers it inappropriate to conduct any meta-analysis.

8 Interpretation of the clinical evidence

The EAC identified a large volume of evidence (N=58 studies) specifically using the GreenLight XPS 180 W console. However, the identified evidence included only 11 comparative studies. 4 of these studies compared different surgical techniques using GreenLight XPS, and this included the only randomised evidence, which compared 24 patients undergoing standard GreenLight PVP with 25 patients undergoing GreenLight PVP using an ejaculatory hood-sparing surgical technique. The remaining 7 studies compared GreenLight PVP with other surgical procedures (TURP, HoLEP, ThuLEP, PAE, open prostatectomy); however duration of follow-up was limited to 12 months in 4 studies, and not explicitly reported in 3 studies. Long-term evidence from single-arm studies demonstrate that improvements in IPSS, QoL, PVR and Qmax are sustained up to 60 months post-operatively when compared to baseline. However, due to the lack of randomised evidence, the EAC is unable to comment on long-term efficacy of GreenLight when compared to other surgical interventions such as HoLEP or TURP.

The majority of studies included high-risk patients within their recruitment (prostate volume greater than 100 ml, preoperative urine retention, high risk of bleeding), but only 4 studies reported high-risk populations exclusively. An additional 4 cohort studies stratified by anticoagulation status, only 1 reported need for transfusions (2 of 422, 0.5%); 1 patient on aspirin, 1 on another antiplatet medication (Meskawi *et al.* 2019). No blood transfusions were

required in the cohort study by Lee *et al.* (2016) (n=384 patients), Knapp *et al.* (2017) (n=373 patients), Eken and Soyupak (2018) (n=233 patients). Only one retrospective cohort study (n=332 patients) reported that duration of catheterisation and length of stay were significantly different between patients with and without preoperative urine retention (Goueli *et al.* 2017). One retrospective cohort study (n=1,031 patients) by Campobasso *et al.* (2020) which used a mixture of standard PVP and anatomical PVP, reported capsular perforation in 8 patients and blood transfusion in 4, however all these events occurred in patients with low prostate volume (less than 100 ml). Whereas the cohort study by Meskawi *et al.* (2017) conducted exclusively in patients with prostate volume greater than 100 ml, reported increasing retreatment rates (0.9%, 5.4%, 9.3%, 2.4% at 1, 2, 3, and 4 years respectively), and reported that retreated patients were more likely to have larger prostate volume.

The proportion of patients undergoing GreenLight intervention as a day-case procedure was reported in four studies, ranging between 36.5% and 90%. There was concensus from the Clinical experts that day-case GreenLight PVP procedures are feasible, however wide variability in the proportion of GreenLight procedures conducted as day-case procedures were estimated by the Clinical experts in line with the published literature; one expert estimated 25% of procedures were conducted as day-case, one expert estimated 40% to 60%, five experts estimated between 80% to 90% (EAC Correspondence Log, 2022). Patients with high anaesthetic risks, frailty, social reasons, co-morbidity status or requiring conversion to another procedure are considered most likely to require longer hospitalisation or be unsuitable for day-case procedure (EAC Correspondence Log, 2022).

Cases of TUR syndrome are rare, with only 1 case recorded across all 56 studies. However, 11 studies reported patients experiencing capsular perforation ranging between 0.1 and 5.6%, and blood transfusions in up to 2.2%.

8.1 *Integration into the NHS*

The majority of identified evidence reported the use of Greenlight XPS in high-risk patient groups. Only one retrospective cohort study was conducted in a UK setting, comparing outcomes between day-case and non-day-case procedures. There is consensus from the Clinical experts with 9 of 11 agreeing that GreenLight XPS can be performed as a day-case procedure or is associated with a reduced hospital stay (EAC Correspondence Log, 2022)

Four experts stated that lack of training is a potential barrier to adoption across the wider NHS (EAC Correspondence Log, 2022).

The GreenLight XPS IFU states that everyone in the room is required to wear protective eyewear. Laser safety precautions for the GreenLight XPS are specific to the wavelength of its green light (532 nm). Safety equipment and signage used in other forms of laser therapy (for example, HoLEP) are not adequate for use with GreenLight, and provider Trusts may have to invest in additional safety equipment on the advice of their Laser Safety Officer. Protective measures (for example, googles per staff member in the room during a GreenLight procedure, and signage if moving GreenLight to day-case theatre settings) should be considered in economic modelling.

Six of the eleven contacted Clinical experts stated that they currently use the GreenLight device for BPH surgery, three have never used the device, one had previous experience with the device and one did not describe level of experience with GreenLight (EAC Correspondence Log, 2022). The EAC has confirmed that the device is still available on NHS Supply Chain.

8.2 *Ongoing studies*

No ongoing studies were identified by the Company Submission. Four ongoing clinical trials were identified within the original assessment report: one is considered out of scope due to GreenLight vapo-enucleation procedure used as the intervention, two were completed with related publications (Ghobrial *et al.* 2020; Fainberg *et al.* 2017 as an abstract only) and the study outcome of the remaining one was unknown (NCT02293759; estimated study completion September 2016) and is included within Appendix C2.

The guidance review report identified 12 ongoing studies. Of these, one study was excluded as a duplicate; three were included within the original assessment report; two were considered out of scope due to the use of Greenlight in GreenLEP (NCT03305861) and vaporesection laser prostatectomy (NCT03318991) interventions with no PVP comparator arm. Two studies have completed with published results (Abolazm *et al.* 2020; Abouelenein *et al.* 2021 available as abstract only). Four studies identified by the guidance review have been included within this ARU; two are ongoing and one status is unknown included within Appendix C2; one is completed with no associated publication identified, Appendix C1.

The EAC conducted an updated search via clinicaltrials.gov.uk on 09/12/2021 using the search terms 'GreenLight'; 'PVP'; 'photovaporisation'; 'photovaporization'. Search term 'PVP' was excluded due to the number of results produced (n=434) even with active or unknown status filters applied (n=177) and the use of 'photovaporisation' or 'photovaporization' did not retrieve any additional studies not identified from the search using 'GreenLight'. The EAC searches identified 32 studies; 28 excluded as they were out of scope (n=19), duplicated (n=6) or had results published (n=3) (Ghobrial *et al.* 2020; Azizi *et al.* 2021; GOLIATH study). Four additional ongoing trials were identified as in scope and included within Appendix C2.

The literature search also identified a further four international studies; two actively recruiting and two completed without publication although GreenLight XPS was not specified as the interventional green laser device in one of these.

In total, 11 ongoing studies were identified and 4 completed with no associated publications identified as of 09/12/2021.

9 Economic evidence

9.1 *Published economic evidence*

Search strategy and selection

The Company did not submit a separate economic search strategy. The Newcastle EAC did not carry out a separate search for economic literature. No search filters, for example, study design or other filters were applied to the Newcastle EAC's clinical evidence search so that any relevant economic evidence retrieved by the search would be included in the search results (Appendix A2). One economics database was searched IDEAS/RePEC (via https://ideas.repec.org) (searched on 30 November 2021, Appendix D). The research results for this database were imported into the same EndNote X.9 library created for the clinical evidence searches so that the Newcastle EAC only had to sift one amalgamated de-duplicated library of search results. Year of publication limits were applied to cut down on the sifting burden and to avoid duplication of effort with what had been screened for the earlier version of this guideline.

Published economic evidence review

From its independent literature search, the Newcastle EAC identified a total of six economic studies, Table 16. None of the identified studies were conducted in the UK or within an NHS setting. Three studies were set in Canada, one in France, one in the USA, and one in Colombia. All studies used a hospital payers' perspective. All six studies included GreenLight XPS with TURP or HoLEP as comparators with four of the six also including other treatment options considered out of scope for this review:

- Ulchaker and Martinson (2018) included Rezum, Urolift, Prostiva and pharmacotherapy;
- Mathieu *et al.* (2017) included open prostatectomy;
- Brown *et al.* (2019) included prostatic artery embolisation;

- Erman *et al.* (2018) compared eight strategies of intervention with GreenLight XPS, TURP and pharmacotherapy.

No study reported high-risk groups exclusively. One of the studies included in the economic evidence was also included within the clinical evidence (Mathieu *et al.* 2017). Studies were appraised using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) Checklist (Husereau *et al.* 2013) in Appendix E.

Table 16: *Summary of economics studies identified.*

Study reference	Methods and perspective	Population	Intervention(s)	Clinical and cost parameters	Summary results	EAC comments
Brown *et al.* (2019) Canada	Cost-comparison analysis of three interventions, plus probabilistic sensitivity analysis using Monte Carlo simulation, from Canadian hospital perspective.	Chart review of 258 patients undergoing TURP (n=209), PVP (n=29) or PAE (n=28) at single centre between April 2015 and March 2017.	TURP, GreenLight PVP, PAE.	Clinical parameters included age, and length of stay (no other parameters explicitly reported). Cost parameters were micro-costed and included costs across hospital cost centres: pre-admission, operating room or angiography suite, anaesthesia, medical imaging and post-anaesthesia care, inpatient, and pharmacy.	Difference in total costs between PVP and TURP not significant (p=0.072) with the total cost of PVP as US$2,146 compared with TURP total cost of US$1,652. PSA showed TURP to be optimal strategy in 24% of cases compared to 8% with PVP (68% with PAE).	PAE comparator out of scope. No significant difference in costs between PVP and TURP.
Caicedo *et al.* (2019) Colombia	Markov model using 6-month cycles over a 2-year period, includingfour health states following treatment with PVP or monopolar TURP with	1,000 simulated patients over the age of 50 years with LUTS secondary to BPE with IPSS ≥10, normal PSA, Qmax ≤15 undergoing TURP or PVP.	TURP, GreenLight PVP.	Clinical parameters included probabilities of reoperation with PVP and TURP, and utilities of PVP, TURP, re-operation, re-	PVP was more cost-effective than TURP with an ICER of US$4,452.81 per QALY gained. Deterministic sensitivity analysis also showed PVP was more likely to be cost-effective, and	PVP more costly but more cost effective than TURP.

Study reference	Methods and perspective	Population	Intervention(s)	Clinical and cost parameters	Summary results	EAC comments
	deterministic and probabilistic sensitivity analysis also used, from Colombian healthcare perspective.			intervention, medical management, being asymptomatic, and urinary incontinence.. Costs included were direct costs of the surgical interventions.	probabilisic sensitivity analysis showed PVP to be more expensive but more effective than TURP.	
Erman *et al.* (2018) Canada	Microsimulation decision analytic model of eight treatment strategies including PVP, TURP, pharmacotherapy, and combinations of these, from Canadian public payer perspective over a lifetime horizon.	250,000 simulated patients with a mean age of 65 years with moderate-to-severe LUTS with presumed BPE undergoing medical or surgical therapy. Baseline characterisitcs (mean): prostate volume 53 ml, IPSS 16, PSA 3.8 ng/mL.	i) upfront PVP; ii) 5-ARI followed by delayed PVP; iii) α-blocker with delayed PVP; iv) combined therapy, 5-ARI & α-blocker, with delayed PVP; v) upfront TURP; vi) 5-ARI followed by delayed TURP; vii) α-blocker with delayed TURP; viii) combined therapy, 5-ARI & α-blocker, with delayed TURP.	Clinical parameters include starting age, IPSS, prostate volume, PSA level, IPSS progression per cycle for each pharmacotherapy agent, effects of BPH surgery on IPSS, and recovery period for BPH related surgeries. Cost parameters include costs of pharmacotherapy, surgical interventions, adverse events, and physician	Upfront surgical interventions (TURP at CAD$12,973 per person and PVP at CAD$11,959 per person) were most expensive, but most cost-effective with ICERs of CAD$29,066 and CAD$14,069 respectively. Upfront pharmacotherapy with delayed PVP treatment options were more cost-effective than upfront pharmacotherapy with delayed TURP (dominated).	Standard of care assumed to include pharmacotherapy in first treatment intervention. PVP more costly than TURP, however TURP was more cost-effective.

Study reference	Methods and perspective	Population	Intervention(s)	Clinical and cost parameters	Summary results	EAC comments
				visit, diagnostic and laboratory costs for BPH-LUTS..		
Masucci *et al.* (2018) Canada	Descriptive costing study from Canadian hospital perspective.	222 patients treated for BPH with GreenLight PVP, bipolar TURP or TURP at a single centre between September 2013 and 30 September 2015†. 202 patients included in analysis due to the first 10 cases per surgeon removed to avoid bias from technology learning curve.	GreenLight PVP (n=56), bipolar TURP (n=29), and TURP (n=118).	Clinical parameters included age, anticoagulation therapy, past medical therapy for BPH, prostate cancer status, median lobe involvement, urinary retention at time of surgery, previous TURP, Charlson Comorbidity Index, number of procedures completed as an outpatient, number of procedures completed as an inpatient, distance to clinic, time spent in operating room, number of laser fibres used (GreenLight only). Cost parameters	Total costs were CAD$3,836 (95% CI: $3,538 to $4,137) for PVP, CAD$4,978 (95% CI: $4,321 to $5,637) for bipolar TURP, and CAD$4,963 (95% CI: $4,701 to $5,226) for TURP. Total costs also reported separately for inpatient procedures, and day-case procedures, and costs associated with readmission reported. Cost savings driven by reduced readmissions and length of stay (including day-case procedures).	Reporting of patient numbers and visits not clear “202 patients corresponding to 203 visits” were included. Authors reported that three of seven patients undergoing TURP as a day-case, were undergoing revisions of a previous TURP procedure. PVP cost saving compared to TURP.

Study reference	Methods and perspective	Population	Intervention(s)	Clinical and cost parameters	Summary results	EAC comments
				include cost of labour, patient supplies, drugs, cost of fibre for GreenLight, cost of resecting loop for TURP, cost of Olympus plasma button, costs for equipment, building and grounds, and hospital overheads.		
Mathieu *et al.* (2017) France	Cost-comparison analysis of four surgical interventions, from French hospital perspective.	237 patients undergoing surgical intervention for BPH between January 2012 and June 2013 across nine French institutions (7 public, 2 private), each recruiting 20 to 30 consecutive patients. Patients met criteria for surgery using guidelines of either EUA or the French Association of Urology. Patients with prostates ≥80 ml, with urinary retention and on anticoagulation therapy were included. Baseline characteristics (mean):	GreenLight PVP (n=51); TURP (n-99) [only used as a comparator in patients with a prostate volume <80 ml]; HoLEP/ThuLEP (n=64); open prostatectomy (n=23) [only used as a comparator in patients with a prostate volume ≥80 ml; out of scope].	Clinical parameters include age, prostate volume, ASA score, urinary retention and catheter use, platelet aggregation inhibitor or anticoagulation, operative time, operative time per gram of prostate, length of stay (also stratified by prostate volume), and complications.	Mean total costs: €2,659 (prostate volume <80 ml) and €2,501 (prostate volume ≥80 ml) for PVP; €2,168 (prostate volume <80 ml only) for TURP; €2,007 (prostate volume <80 ml) and €2,702 (prostate volume ≥80 ml) for HoLEP/ThuLEP; €3,375 (prostate volume ≥80 ml only) for open prostatectomy. PVP and HoLEP/ThuLEP associated with shorter LoS compared to TURP, so despite increased upfront technology	Comparator open prostatectomy, out of scope. HoLEP and ThuLEP interventions not reported exclusively. Baseline characteristics of groups comparable aside from greater prostate volume in patients receiving open prostatectomy and higher rates

Study reference	Methods and perspective	Population	Intervention(s)	Clinical and cost parameters	Summary results	EAC comments
		age 71.7 years, prostate volume 65.5 ml.		Cost parameters were not reported separately, but assumed to include all costs contributing to total cost of hospitalisation.	costs, could be cheaper overall.	of anticoagulation therapies used in HoLEP and PVP groups. EAC notes reporting of prostate volume does not have consistent units in Table 4 (includes mL and g). PVP cost saving compared to TURP and HoLEP/THuLEP.
Ulchaker and Martinson (2018) USA	Markov model comparing six treatments for BPH over two-year time horizon with six-month cycles, and uncertainty addressed with probabilistic sensitivity analysis (1,000 samples of parameters with 100 individuals in each sample to provide 100,000 simulations). US	Simulated patients undergoing therapy with prescription drugs, a minimally invasive therapy, or invasive therapy. Baseline characteristics not reported.	In scope: GreenLight PVP; TURP Out of scope: combination pharmacotherapy (5-ARI and α-blocker); Prostiva; Rezum; UroLift.	Clinical parameters include change in IPSS, return of LUTS, incontinence, incidence of adverse events (*de novo* erectile dysfunction, stricture, contracture, stenosis, acute urinary retention, urinary tract infection. Costs	Total costs: US$5,099 for PVP and US$5,181 for TURP. ICER at 2 years was $83 in favour of PVP. TURP was more expensive than PVP about 59% of the time, and more effective about 73% of the time.	Prostiva, Rezum, UroLift and drug comparators out of scope. PVP cost saving compared with TURP, but TURP more cost effective.

Study reference	Methods and perspective	Population	Intervention(s)	Clinical and cost parameters	Summary results	EAC comments
	health care payer perspective.			include therapy and procedure costs, costs of treating adverse events.		
Abbreviations: PVP, photoselective vaporisation of the prostate; PAE, prostatic artery embolisation; TURP, transurethral resection of the prostate; PSA, prostate specific antigen; IPSS, international prostate symptom score; LUTS, lower urinary tract symptoms; BPE, benign prostatic enlargement; QALY, quality adjusted life year; ICER, incremental cost-effectiveness ratio; 5-ARI, 5-alpha reductase inhibitor; BPO, benign prostatic obstruction; EUA, European Urology Association; LoS, length of stay; CAD, Canadian dollars; US, United States of America; HoLEP, holmium laser enucleation of the prostate; ThuLEP, thulium laser enucleation of the prostate; BPH, benign prostatic hyperplasia; †As reported						

Results from the economic evidence

Two of the six studies found GreenLight XPS to be cost-saving compared with TURP (Masucci *et al.* 2018, Ulchaker and Martinson 2018). Cost savings were driven by reduction in readmissions and length of stay including performing day-case procedures. One study found GreenLight to be more cost-effective than TURP (Caicedo *et al.* 2019), whereas two studies reported TURP to be more cost-effective (Erman *et al.* 2018, Ulchaker and Martinson 2018). One study reported GreenLight to be more costly than TURP and HoLEP or ThuLEP in patients with prostate volume less than 80 ml, but cost-saving compared to HoLEP or ThuLEP in patients with prostate volume greater than 80 ml (Mathieu *et al.* 2017). Age, and distance to the hospital were not considered predictors of cost (Masucci *et al.* 2018). Comorbidity, as assessed using the Charlson Comorbidity Index, is an independent predictor of cost (Masucci *et al.* 2018).

Masucci *et al.* (2018) reported on a Canadian cohort undergoing GreenLight PVP or monopolar or bipolar TURP. Total per patient costs were reported (Canadian dollars) of $3,836 [95% CI: $3,538 to $4,137] for PVP; $4,978 [$4,321 to $5,637] for bipolar TURP; $4,963 [$4,701 to $5,226] for monopolar TURP.

Mathieu *et al.* (2017) also reported total procedure costs for a French cohort undergoing GreenLight PVP or HoLEP or ThuLEP. TURP was used as a comparator in patients with a prostate volume less than 80 ml. Open prostatectomy was used as a comparator in patients with a prostate volume equal or greater than 80 ml and is considered out of scope of this review. Costs were reported by prostate volume (less than 80 ml, greater than or equal to 80 ml). Per patient procedure costs were €2,659 (SD €1,397) for PVP compared with €2,168 (SD €596) for TURP and €2,007 (SD €549) for HoLEP or ThuLEP for prostates less than 80 ml. In prostates equal to or greater than 80 ml, PVP costs were €2,501 (SD €540) and HoLEP or ThuLEP costs were reported as €2,702 (SD €783). PVP was identified to be significantly more expensive than TURP and HoLEP or ThuLEP in prostates less than 80 ml however, this was not observed in the larger prostate group. In addition, the

standard deviation for PVP in the smaller prostate group is considerably larger than the comparators. Costs were driven by the higher initial device costs and consumables and authors noted shorter length of stays with PVP, HoLEP or ThuLEP compared to TURP that may provide cost savings over a longer time point.

Caicedo *et al.* (2019) found GreenLight XPS to be cost-effective compared with TURP with an ICER of $4,452 (US dollars) per QALY gained over a two-year horizon.

Ulchaker and Martinson (2018) used a Markov model to compare six interventions, four of which are considered out of scope for this review (combination pharmacotherapy, Prostiva, Rezum, and Urolift). Total costs (US dollars) over a two-year period were reported as $5,099 for PVP and $5,181 for TURP. Probabilistic sensitivity analysis identified TURP as more expensive 59% of the time and more effective 73% of the time. Authors reported an ICER of $83 per additional point reduction in IPSS, favouring GreenLight XPS to TURP.

One study found no significant difference in total costs (US dollars) between GreenLight PVP, $2,146 (SD $563) and TURP, $1,652 (SD $692) (p=0.072) (Brown *et al.* 2019) although indirect costs were higher in GreenLight XPS. The sample size for patients undergoing GreenLight XPS was much lower (n=28) compared with TURP (n=209).

Erman *et al.* (2018) modelled eight intervention strategies over a patient lifetime horizon including upfront pharmacotherapy (α-blocker, 5ARI, or combination) followed by surgical interventions (TURP or GreenLight PVP) upon failure, compared with TURP or GreenLight PVP as the initial treatment. Upfront surgical TURP and PVP interventions were the most expensive (Canadian dollars) and cost-effective with ICERs of $29,066 and $14,069 respectively. These strategies are not considered to be standard of care within the NHS.

9.2 *Company de novo cost analysis*

Economic model structure

For this guidance update, the EAC considered the original decision tree model updated by Birmingham and Brunel EAC during development of the original Assessment Report (EAC Assessment Report, 2015), provided in Microsoft Excel. In brief, a patient undergoes an intervention (Greenlight XPS compared with TURP and HoLEP) as either a day-case, or inpatient. Following this, the endpoints are the occurrence of no complications, grade two complications, or grade three complications, by six months after the intervention. This time horizon remains appropriate for safety outcome measures, as most complications would still be expected to occur in this period, however a longer time horizon would be beneficial for efficacy outcomes.

The Company made a number of assumptions in their Economic Submission, some of which were discussed in the Assessment Report by Birmingham and Brunel EAC. Any assumptions not discussed by Birmingham and Brunel EAC have been assumed by Newcastle EAC to have been considered appropriate at the time of the original assessment. In summary, the Company estimated the proportions of patients undergoing interventions as a day-case (versus inpatient) based on Hospital Episodes Statistics (HES) data, and provided other sources to be used in sensitivity analysis. Birmingham and Brunel EAC considered the use of HES data would have been appropriate if the GreenLight intervention was standard practice, but as it was not, requested and received academic in confidence data from the GOLIATH trial; which still remains the only randomised evidence of GreenLight compared with TURP. Birmingham and Brunel EAC agreed with the Company's application of mean reference costs for most inpatient stays, assuming they stayed for five days or less, and applied excess bed day costs for each additional day stayed.

The Birmingham and Brunel EAC base case included the possibility of patients to experience more than one adverse event, which was presented in the original Assessment Report. The Newcastle EAC consider that this approach remains valid.

Economic model parameters

During exploration of the model, the EAC noted errors in some of the clinical parameters applied in the Birmingham and Brunel EAC base case presented in the original Assessment Report, however the impact of these on total cost differences between arms were minimal. For example, for each of the three intervention arms, the mean numbers of grade two and grade three complications per patient had been transposed. These were estimated correctly from the source (Bachmann *et al.* 2014) and listed correctly in Table 16 of the original Assessment Report, but applied incorrectly in the Excel model. For patients experiencing non-acute incontinence as a complication, the model incorrectly assumed that incontinence pads were used for 184.5 days which should have been 182.5 days (1 pad per day for 6 months; 365/2). The EAC also noted a typographical error in the economic model, in which it was stated that 2.37% of patients undergoing GreenLight treatment had a hospital length of stay less than 5 days; the EAC assumes that this was meant to read greater than 5 days. The EAC also noted a typographical error in Table 16 of the original Assessment Report, in which the average cost of treating adverse events in the hospital per patient was £937.82 in the GreenLight arm, and £973.82 in the TURP arm of the model. NHS Reference Costs (via Health Resouce Group codes) do not differentiate between treatment type and the Newcastle EAC notes that £937.82 was applied consistently in the model across both arms. The EAC also noted that some model parameters were hidden in the Microsoft Excel model (for example, life years of HoLEP device, and amortisation rate).

Clinical parameters and variables

The Newcastle EAC reports that there is no additional randomised evidence comparing GreenLight to HoLEP or TURP. Therefore, clinical outcomes (including safety and efficacy outcomes and operation times) included in the model are the same of the GOLIATH trial (comparing GreenLight with TURP), and unchanged from the original Assessment Report.

The mean lengths of stay applied in the original economic model were 10.36 days for HoLEP and GreenLight, and 10.65 days for TURP; with 2.37% and 5.41% of patients (in GreenLight or HoLEP and TURP arms respectively)

staying in hospital beyond an average length of stay (the trim point assumed for HRG costings) of 5 days. The Newcastle EAC notes that currently available procedure (OPCS) codes combine procedures together, however from NHS activity reports from 2019/20, the mean length of stay for TURP (based on 11,420 admissions with primary procedure code M65.3 Endoscopic resection of prostate not elsewhere classified, which combines mono- and bi-polar TURP) is 2.3 days, and 1.6 days for GreenLight or HoLEP (based on 3,943 admissions with primary procedure code M65.4 Endoscopic resection of prostate using laser, which combines GreenLight and HoLEP). The procedure costs included in the economic model are based on HRG codes, for GreenLight, TURP and HoLEP, with an assumed average length of stay that is significantly shorter than ten days. As none of the newly available evidence reports the number of patients staying in hospital beyond five days, the Newcastle EAC has removed excess bed days from the economic model (by setting the excess bed day cost to zero).

Resource identification, measurement and valuation

The Company confirmed that the cost of GreenLight was unchanged from the original Assessment Report (EAC Correspondence Log, 2022), however due to lack of available Healthcare Resource Group (HRG) codes (which currently do not differentiate HoLEP and GreenLight procedures) the Newcastle EAC considered it incorrect to keep the cost of GreenLight the same and only increase the cost of the comparators (HoLEP, TURP) by inflation. For consistency the Newcastle EAC used technology costs for GreenLight, TURP and HoLEP which were published in the recent assessment report of a different BPH technology (Rezum) (EAC Assessment Report, 2019). All updated costs are described in Table 17.

The EAC notes that protective eyewear is required for each member of staff in the room during GreenLight and HoLEP procedures. Protective eyewear is specific to the wavelength of laser light used, and eyewear suitable for HoLEP is unsuitable for Greenlight and vice versa. Clinical experts stated that the number of staff present during a GreenLight procedure ranged between 5 and 12, however that the same number would be present during HoLEP

procedure. A Laser Protection Adviser has advised that the costs of eyewear will be similar between GreenLight and HoLEP procedures (EAC Correspondence Log, 2022). Given the reusable nature of goggles and their average lifetime being five years, the EAC considered the additional costs of protective eyewear to be negligible, and therefore did not add these to the consumable costs of the economic model.

Table 17: Cost parameters used in the Company's model and changes made by the EAC

Cost parameter	Unit cost (Original model)	Unit costs (Updated 2021)	Source (Updated 2021)
Unit cost per day-case procedure	£1,544.00	£2,474.00	NHS Reference Costs 2019-20; Day-case LB25F (Transurethral Prostate Resection Procedures with CC Score 0-2)
Unit cost per inpatient procedure	£2,485.00	£3,420.00	NHS Reference Costs 2019-20; Elective LB25F (Transurethral Prostate Resection Procedures with CC Score 0-2)
Unit cost per outpatient follow up appointment	£101.00	£112.00	NHS Reference Costs 2019-20; Total Outpatient Attendance; Service Code 101 Urology (Consultant-led)
Unit cost per excess bed day	£294.00	£0	The average length of stay associated with GreenLight/HoLEP and TURP were 10.36 and 10.65 days respectively in the original assessment report. NHS Activity reported in 2019/20 reports average length of stay of 1.6 and 2.3 days for GreenLight/HoLEP and TURP respectively. No new evidence reports the proportion of patients staying more than 5 days, therefore excess bed days are removed in the updated model.
Greenlight			
Total cost of consumables	£550.00	£540.00	Cost used in Rezum EAC Assessment Report, 2019 "Rezum for treating lower urinary tract symptoms secondary to benign prostatic hyperplasia". Company have confirmed that the capital cost of the console is not included (as per original economic model), cost per fibre with additional fibres per patient provided free of charge (EAC Correspondence Log, 2022). Cost does not include saline for cooling the laser, its inclusion would have limited impact on total costs.
TURP			
TURP Mono-loop	£50.00	£52.60	Costs used in EAC Assessment Report, 2019 "Rezum for treating lower urinary tract symptoms secondary to benign prostatic hyperplasia". In line with the approach taken in the Rezum Assessment Report, the Newcastle EAC also changed proportion of procedures using bipolar TURP from 50% to 75%.
TURP Bi-loop	£180.00	£189.29	
Glycine fluid	£5.08	£5.34	
Ellik evacuator	£20.00	£21.04	
Saline for bladder irrigation	£5.08	£5.72	Inflated from 2015 to 2020 using Consumer Price Index table released 15/12/2021 (Table 9 L528 Health; 112.6/100) Model assumes that 50% of patients undergoin TURP, require 7 days of saline bladder irrigation for 2.55 days.
HoLEP			
Single use fibre	£160.00	£189.34	Costs/parameters used in EAC Assessment Report, 2019 "Rezum for treating lower urinary tract symptoms
Reusable fibre	£700.00	£736.34	
Fibre stripper and cleaver	£50.00	£52.60	

Cost parameter	Unit cost (Original model)	Unit costs (Updated 2021)	Source (Updated 2021)
Morcellator cutting blade	£200.00	£210.38	secondary to benign prostatic hyperplasia". Model assumed that 50% of HoLEP fibres are single use.
Suction tubing	£20.00	£21.04	
Omni-jug	£7.00	£7.36	
Ellik evacuator	£20.00	£21.04	
HoLEP device	Average of: £100,000.00 £130,000.00 £50,000.00 £70,000.00	£92,042.12	
HoLEP morcellator	£30,000.00	£31,557.30	
Patients treated per year	25	250	
Useful life years	5	10	
Depreciation	3.5%	Linear, over useful life years	Original model applied depreciation in line with discount rate. EAC notes that HoLEP annual capital costs are (£92,042.12 + £31,557.30)/10 = £12,359.94 assuming linear depreciation over 10 years (per-procedure cost of £49.44 assuming 250 procedures per year per device). This element of the cost not subject to discount as it arises in year 1 of the time horizon for each patient.
Capital cost per procedure	£1,040.96	£49.44	*Calculated from above rows.*
Treatment of adverse events			
Moderate incontinence (primary care)			
GP appointment	£46.00	£33.00	PSSRU 2020/21; GP consultation of 9.22 minutes, including direct care.
Course of Ciprofloxacin (500mg, 20 tablet pack)	£1.46	£4.38	BNF 2021; drug tariff price for 2 packs of 10 tablets.
Pad	£0.34	£0.38	Inflated from 2015 to 2020 using Consumer Price Index table released 15/12/2021 (Table 9 L528 Health; 112.6/100) A total of 182.50 pads used over 6 month period (365/2 days).
Physiotherapist appointment	£37.00	£38.00	PSSRU 2020/21; Hospital based physiotherapist band 5 (1 hour).
Total cost of treatment	*£147.06*	*£144.73*	*Caculated from above rows.*
Non-acute urinary retention (primary care)			
GP appointment	£46.00	£33.00	PSSRU 2020/21; GP consultation of 9.22 minutes, including direct care.
Catheter	£1.30	£1.62	Inflated from 2011 to 2020 using Consumer Price Index table released 15/12/2021 (Table 9 L528 Health; 112.6/90.6) Applied to 39% of patients with non-acute UTI complication.

Cost parameter	Unit cost (Original model)	Unit costs (Updated 2021)	Source (Updated 2021)
Course of Ciprofloxacin (500mg, 20 tablet pack)	£1.47	£4.38	BNF 2021; drug tariff price for 2 packs of 10 tablets.
Total cost of treatment	*£48.77*	*£39.00*	*Calculated from above rows*
Non-acute bleeding (primary care)			
GP appointment	£46.00	£33.00	PSSRU 2020/21; GP consultation of 9.22 minutes, including direct care.
Course of trimethoprim (200mg, 14 tablet pack)	£1.31	£2.71	BNF 2021; drug tariff price
Total cost of treatment	*£47.31*	*£35.71*	*Calculated from above rows*
Non-acute urinary tract infection (primary care)			
GP appointment	£46.00	£33.00	PSSRU 2020/21; GP consultation of 9.22 minutes, including direct care.
Midstream urine sample	£0.58	£0.66	Inflated from 2014 to 2020 using Consumer Price Index table released 15/12/2021 (Table 9 L528 Health; 112.6/98.1). Applied to 39% of patients with non-acute UTI complication.
Dipstick test	£0.11	£0.13	Inflated from 2015 to 2020 using Consumer Price Index table released 15/12/2021 (Table 9 L528 Health; 112.6/98.1) Applied to 56% of patients with non-acute UTI complication.
Course of trimethoprim (200mg, 14 tablet pack)	£1.00	£2.71	BNF 2021; drug tariff price Applied to 84% of patients with non-acute UTI complication.
Total cost of treatment	*£47.13*	*£35.61*	*Calculated from above rows.*
Adverse events (secondary care)			
Acute urinary retention	£1,238.63	£1,941.79	NHS Reference Costs 2019-20, codes and categories matched to original Assessment Report. Weighted average: LB16E (Urinary Incontinence or Other Urinary Problems, with Interventions, with CC Score 3-6; non-elective long stay, non-elective short stay), LB16F (Urinary Incontinence or Other Urinary Problems, with Interventions, with CC Score 0-2; non-elective long stay, non-elective short stay).

Cost parameter	Unit cost (Original model)	Unit costs (Updated 2021)	Source (Updated 2021)
Acute stricture	£1,202.71	£1,606.28	NHS Reference Costs 2019-20, codes and categories matched to original Assessment Report. LB29A (Major Open Urethra Procedures, 19 years and over; non-elective short stay, day-case, outpatient)
Acute bleeding	£479.17	£500.13	NHS Reference Costs 2019-20, codes and categories matched to original Assessment Report. Weighted average: LB14Z (Intermediate Endoscopic Bladder Procedures; non-elective short stay, day-case), LB15E (Minor Bladder Procedures, 19 years and over, all settings).
Acute urinary tract infection	£1,060.50	£1,561.48	NHS Reference Costs 2019-20, codes and categories matched to original Assessment Report. Weighted average: LA04N (Kidney or Urinary Tract Infections, without Interventions, with CC Score 13+), LA04P (Kidney or Urinary Tract Infections, without Interventions, with CC Score 8-12), LA04Q (Kidney or Urinary Tract Infections, without Interventions, with CC Score 4-7), LA04R (Kidney or Urinary Tract Infections, without Interventions, with CC Score 2-3), LA04S (Kidney or Urinary Tract Infections, without Interventions, with CC Score 0-1); non-elective short stay, non-elective long stay, day-case.
Average per patient cost of treating adverse events in hospital	*£937.82*	*£1,074.14*	*Calculated weight average of acute retention, stricture, bleeding and UTI using activity and costs from NHS Reference Costs 2019/20.*

Sensitivity analysis

No additional randomised comparative evidence of GreenLight compared with HoLEP or TURP has been published since the original Assessment Report. No additional randomised evidence was available for the different high-risk subgroups (prostate volume greater than 100 ml, patients with preoperative urine retention, or patients at high risk of bleeding). Therefore, the EAC did not update any clinical parameters in the economic model.

Newcastle EAC considers that due to lack of comparative data in the UK there remains significant uncertainty regarding the proportion of patients undergoing prostate intervenitons for BPH as a day-case procedure. Only one single-arm UK study was identified by the EAC literature search, which reported 68% of GreenLight procedures being conducted as day-case procedures (Trail *et al.* 2021), which will be applied in univariate sensitivity analysis. Four Clinical experts agreed with 68% of GreenLight cases being performed as day-case procedures and three Clinical experts were unsure of the proportions (EAC Correspondence Log, 2022). Two additional Clinical experts suggested alternative figures, with one expert noting 90% of GreenLight being performed as day-case and another noting 20% as a more realistic figure (EAC Correspondence Log, 2022). Four Clinical experts advised that 36% and 4% of patients undergoing day-case procedures for HoLEP and TURP respectively, as assumed in the original economic model, remained appropriate (EAC Correspondence Log, 2022). Three additional clinical experts suggested that the proportion undergoing day-case TURP procedures should be higher than 4% (range 4 to 20%). One Clinical expert also suggested higher day-case proportion in patients undergoing HoLEP (range 35 to 60%), and highlighted the study by Lee *et al. (*2018) from a single UK centre, which included 210 patients undergoing HoLEP, 74 (35.2%) of which were discharged as day-cases. One Clinical expert stated that there was too much uncertainty to comment on the proportion undergoing GreenLight, HoLEP or TURP as a day-case procedure. Due to variation across the NHS and uncertainty regarding the proportion of patients undergoing day-case procedures, the EAC applied threshold analysis to determine the proportions of day-cases required for equipoise.

9.3 *Results from the economic modelling*

Base case results

The base case results from the original Assessment Report (EAC Assessment Report, 2015), including corrections and updated costs comparing GreenLight to TURP and HoLEP are shown in Table 18a and Table 19a respectively (additional breakdown of costs including rate of events shown in Table 18b and Table 19b for TURP and HoLEP respectively).

Table 18a: Summary of base case results – GreenLight versus TURP

	Base case results (Original model)			Base case results (Corrected 2022)			Base case results (Updated 2022)		
	GreenLight XPS	TURP	Difference*	GreenLight XPS	TURP	Difference*	GreenLight XPS	TURP	Difference*
Day-case	£555.28	£63.00	£492.28	£555.28	£63.00	£492.28	£889.74	£100.95	£788.79
Inpatient	£1,628.60	£2,473.46	-£844.86	£1,628.60	£2,473.46	-£844.86	£2,190.04	£3,280.45	-£1,090.40
Grade 2 complications	£13.82	£7.46	£6.36	£12.96	£7.25	£5.70	£10.63	£5.47	£5.17
Grade 3 complications	£131.02	£204.49	-£73.47	£139.76	£210.47	-£70.72	£160.07	£241.02	-£80.95
Capital costs	£0.00	£0.00	£0.00	£0.00	£0.00	£0.00	£0.00	£0.00	£0.00
Outpatient follow up	£101.00	£101.00	£0.00	£101.00	£101.00	£0.00	£112.00	£112.00	£0.00
Consumables	£550.00	£145.16	£404.84	£550.00	£145.16	£404.84	£540.00	£181.50	£358.50
Other	£0.00	£45.34	-£45.34	£0.00	£45.34	-£45.34	£0.00	£51.05	-£51.05
Total	**£2,979.72**	**£3,039.91**	**-£60.19**	**£2,987.60**	**£3,045.69**	**-£58.09**	**£3,902.49**	**£3,972.43**	**-£69.94**

* Negative values denote cost-savings for GreenLight when compared with TURP

Table 18b: Breakdown of base case results – GreenLight versus TURP

	GreenLight			TURP			
	Proportion of patients	Cost	Total cost	Proportion of patients	Cost	Total cost	Difference*
Day-case	35.96%	£2,474	£889.74	4.08%	£2,474	£100.95	£788.79
Inpatient	64.04%	£3,420	£2,190.04	95.92%	£3,420	£3,280.45	-£1,090.40
Grade 2 complications	22.06%; 1 per patient *(12% incontinence, 12% non-acute bleeding, 77% UTI)*	£48 *(incontinence £144.73, bleeding £35.71, UTI, £35.61)*	£10.63	14.28%; 1.0741 per patient *(14.8% incontinence, 11.1% bleeding, 74.1% UTI)*	£36 *(incontinence £144.73, bleeding £35.71, UTI, £35.61)*	£5.47	£5.17
Grade 3 complications	13.97%; 1.0667 per patient	£1074	£160.07	20.30%; 1.1053 per patient	£1074	£241.02	-£80.95
Capital costs	100%	£0.00	£0.00	100%	£0.00	£0.00	£0.00
Outpatient follow up	100%	£112	£112.00	100%	£112	£112.00	£0.00
Consumables	Fibre: 100%	Fibre: £540	£540.00	Mono-TURP: 25% BI-TURP: 75% 4 bags glycine (2L each) 100% Elik evacuator	Mono loop: £52.60 Bi-loop: £189.29 Glycine: £5.34 Evacuator: £21.04	£181.50	£358.50
Other	0%	£0.00	£0.00	Saline bladder irrigation: 50%	Saline bladder irrigation: 7 units (£5.72) each, for 2.55 days	£51.05	-£51.05
Total	**£3,902.49**			**£3,972.43**			**-£69.94**
* Negative values denote cost-savings for GreenLight when compared with TURP							

Table 19a: Summary of base case results – GreenLight versus HoLEP

	Base case results (Original model)			Base case results (Corrected 2022)			Base case results (Updated 2022)		
	GreenLight XPS	HoLEP	Difference*	GreenLight XPS	HoLEP	Difference*	GreenLight XPS	HoLEP	Difference*
Day-case	£555.28	£555.28	£0.00	£555.28	£555.28	£0.00	£889.74	£889.74	£0.00
Inpatient	£1,628.60	£1,628.60	£0.00	£1,628.60	£1,628.60	£0.00	£2,190.04	£2,190.04	£0.00
Grade 2 complications	£13.82	£13.82	£0.00	£12.96	£12.96	£0.00	£10.63	£10.63	£0.00
Grade 3 complications	£131.02	£131.02	£0.00	£139.76	£139.76	£0.00	£160.07	£160.07	£0.00
Capital costs	£0.00	£1,040.96	-£1,040.96	£0.00	£1,040.96	-£1,040.96	£0.00	£49.44	-£49.44
Outpatient follow up	£101.00	£101.00	£0.00	£101.00	£101.00	£0.00	£112.00	£112.00	£0.00
Consumables	£550.00	£360.17	£189.83	£550.00	£360.17	£189.83	£540.00	£376.13	£163.87
Other	£0.00	£0.00	£0.00	£0.00	£0.00	£0.00	£0.00	£0.00	£0.00
Total	**£2,979.72**	**£3,830.85**	**-£851.13**	**£2,987.60**	**£3,838.72**	**-£851.13**	**£3,902.49**	**£3,788.06**	**£114.43**

* Negative values denote cost-savings for GreenLight when compared with HoLEP

Table 19b: Breakdown of base case results – GreenLight versus HoLEP

	GreenLight			HoLEP			
	Proportion of patients	Per-procedure cost	Total cost	Proportion of patients	Per-procedure Cost	Total cost	Difference*
Day-case	35.96%	£2,474	£889.74	35.96%	£2,474	£889.74	£0.00
Inpatient	64.04%	£3,420	£2,190.04	64.04%	£3,420	£2,190.04	£0.00
Grade 2 complications	22.06%; 1 per patient *(12% incontinence, 12% non-acute bleeding, 77% UTI)*	£48 *(incontinence £144.73, bleeding £35.71, UTI, £35.61)*	£10.63	22.06%; 1 per patient *(12% incontinence, 12% non-acute bleeding, 77% UTI)*	£48 *(incontinence £144.73, bleeding £35.71, UTI, £35.61)*	£10.63	£0.00
Grade 3 complications	13.97%; 1.0667 per patient	£1074	£160.07	13.97%; 1.0667 per patient	£1074	£160.07	£0.00
Capital costs	100%	£0.00	£0.00	100%	£49.44 (laser: £92,042.12, morcellator £31,557.30, 250 patients per year, device lifespan 10 years)	£49.44	-£49.44
Outpatient follow up	100%	£112	£112.00	100%	£112	£112.00	£0.00
Consumables	Fibre: 100%	Fibre: £540	£540.00	Single use: 50% Reusable: 50%	Single use: £443.03 Reusable: £309.23	£376.13	£163.87
Other	0%	£0.00	£0.00	0%	£0.00	£0.00	£0.00
Total	**£3,902.49**			**£3,788.06**			**£114.43**
* Negative values denote cost-savings for GreenLight when compared with HoLEP							

With updated costs, the EAC has found that GreenLight remains cost-saving when compared with TURP, and slightly cost-incurring when compared with HoLEP. This is due to decreased capital costs (attributed per patient) associated with the increased use (per year) of HoLEP in the updated model, in line with the approach taken in the Rezum EAC assessment report, 2019.

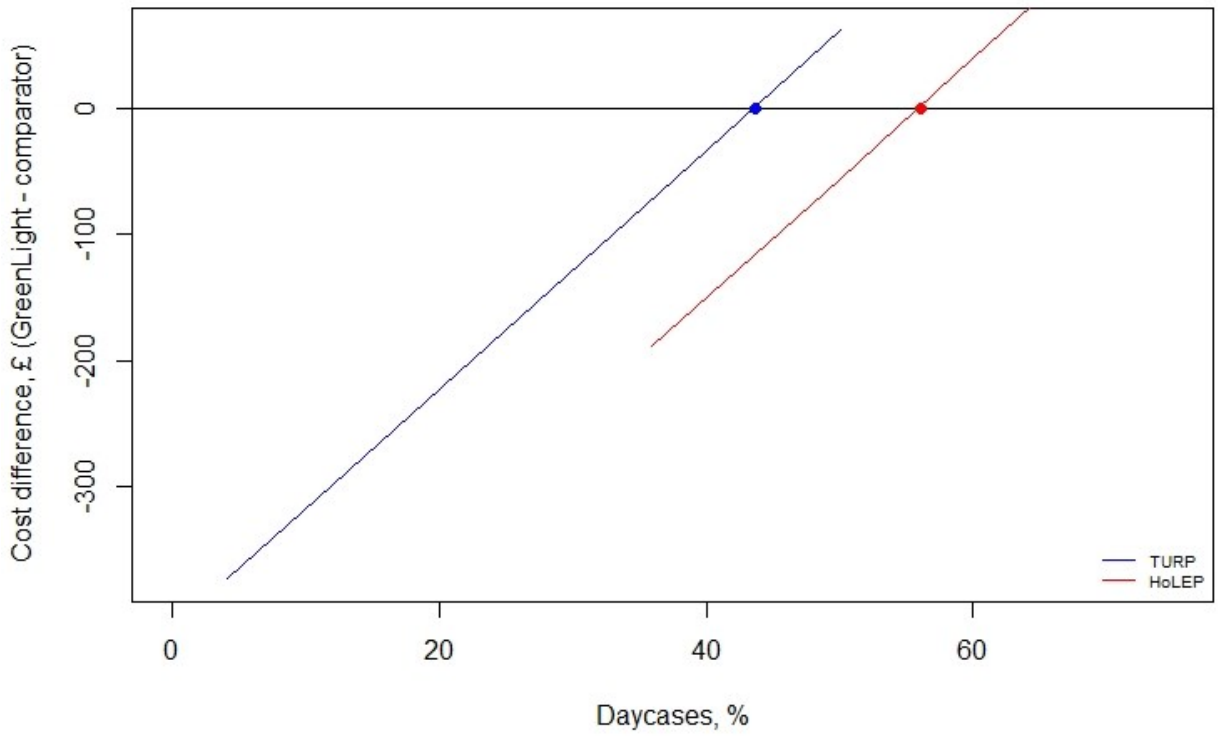
Sensitivity analysis results

Univariate sensitivity analysis demonstrating the impact of day-case procedures rates for GreenLight on cost differences between GreenLight, TURP and HoLEP arms is shown in Table 20. From threshold anlaysis (when maintaining GreenLight day-case procedures at 68%), the proportion of day-case procedures for TURP would have to exceed 43.6% before GreenLight would be considered cost-incurring, Figure 1; this is clinically unlikely. From additional threshold analysis, the proportion of HoLEP being day-case procedures would have to exceed 56% for GreenLight to be considered cost-incurring; this scenario is possible and within the upper range suggested by Clinical experts (EAC Correspondence Log, 2022).

Table 20: Sensitivity analysis and impact on cost per patient across GreenLight, TURP and HoLEP arms.

			Base-case			Sensitivity analysis			
Parameter	Base-case value	Updated value	GreenLight	Comparator	**Difference**	GreenLight	Comparator	**Difference**	EAC comment
Proportion of day-case procedures	GreenLight: 35.96% TURP: 4.08% HoLEP: 35.96%	GreenLight: 68% TURP: 4.08% HoLEP: 35.96%	£3,902.49	TURP: £3,972.43 HoLEP: £3,788.06	**TURP: -£69.94 HoLEP: +£114.43**	£3,599.43	TURP: £3,972.43 HoLEP: £3,788.06	**TURP: -£373.01 HoLEP: -£188.63**	Increasing the proportion of patients receiving GreenLight as a day-case procedure increases cost savings and demonstrates GreenLight to be cost saving when compared to HoLEP (assuming day-case rate for HoLEP remains fixed at 35.96%).

Figure 1: Threshold analysis on the proportion of day-case procedures



9.4 Company de novo cost analysis (new Markov model)

Economic model structure

The EAC received an updated economic model and Submission from the Company (on 23/12/2021), which was based on the cost-consequences model submitted for an alternative technology (Rezum, also manufactuered by Boston Scientific) as an alternative treatment of lower urinary tract symptoms (LUTS), obstructions associated with benign prostate hyperplasia (MTG49, 2020). The Company stated that the reasons for using the updated Markov model were:

- to capture hospital costs more accurately for high-risk patients,
- to apply a more detailed approach to calculating and capturing a range of adverse events,
- to allow the use of 2019/20 costs compared to costs from the original model from 2015,
- due to the flexibility of the Rezum model to select more than one comparator and use GreenLight as the intervention.

The EAC considers that the Company could have incorporated some of these into the original decision tree model submitted for GreenLight within MTG29 (see Section 9.2). However, the EAC considers that the main benefit of using the Markov model is the ability to model surgical retreatment (potentially with a different intervention) and long-term costs.

The updated model (provided in Microsoft Excel) was only partially executable (Visual Basic errors required debugging, a number of cells contained "?NAME" or "N/A" errors when modelling some scenarios). Following review of both the updated model and the Economic Submission, the EAC sent the Company two lists of questions (on 23/03/2022 and 29/03/2022) seeking clarification and explanation regarding the model structure, assumptions and parameters. The Company responded by submitting version 2 of the updated model and updated Economic Submission (on 01/04/2022; EAC

Correspondence Log, 2022). The Company summarised the changes as follows:

- removed protection from all model sheets to allow modification to input parameters;
- modified formulae for erectile dysfunction (ED) outcome such that to avoid error messages when ED was not selected in the Settings worksheet;
- changes to adverse event values across arms;
- addition of costs associated with saline bladder irrigation with both mono- and bi-polar TURP;
- additional scenario where ED was selected.

The updated model (version 2) remained only partially executable. The EAC sent an additional list of queries to the Company (on 04/04/2022) after it identified a number of discrepancies between the Submission and model, and between worksheets within the model (EAC Correspondence Log, 2022). The Company submitted a further revised version of the model and Economic Submission (version 3) on 06/04/2022. However, as agreed with NICE, due to tight timelines the EAC did not accept any further revised models or Submissions. The remainder of the EAC's critique focused on version 2 of the model and Economic Submission (received 01/04/2022), which were critically appraised by the EAC using the Drummond checklist (Drummond *et al.* 1996), Appendix E2.

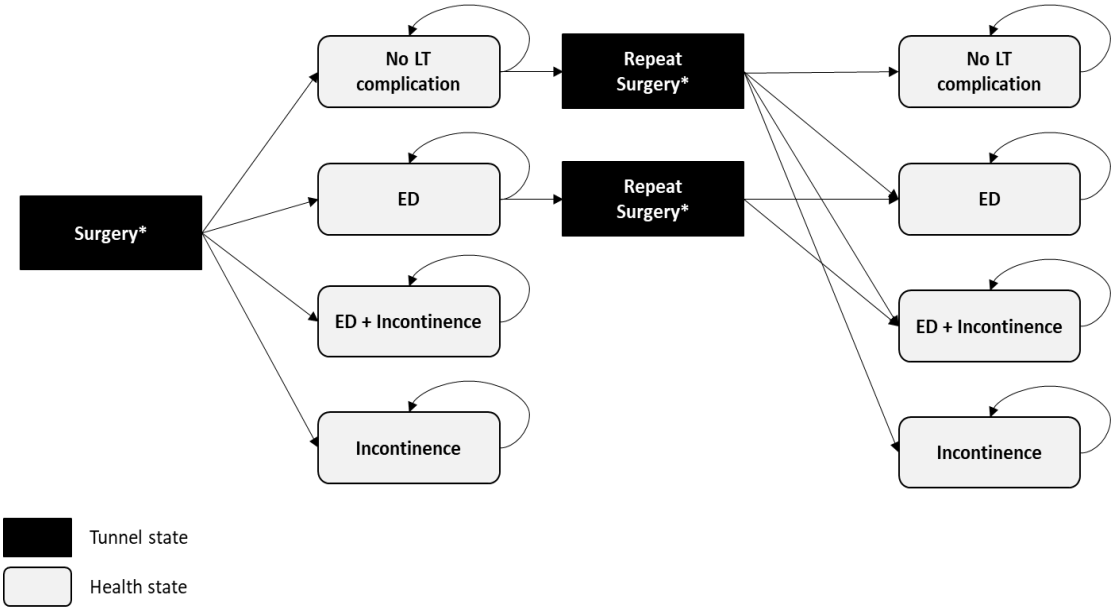
The updated model, provided in Microsoft Excel, employs the same Markov model structure as used in the Rezum assessment, Figure 2, with the same time horizon of four years and a cycle length of three months. The Company confirmed (on 06/04/2022) that their updated Economic Submission stated a time horizon of five years in error (EAC Correspondence Log, 2022). The EAC note the Company justified their choice of time horizon and cycle length on the availability of clinical data at the time of adapting the model in 2020,

suggesting that retreatment rates for GreenLight, TURP, and HoLEP are relevant and multiple retreatment procedures within this timeframe are rare. Six Clinical experts agreed that multiple retreatment procedures within four years are rare (EAC Correspondence Log, 2022). One Clinical expert noted that retreatment may occur 'early' (within one to two years) or 'late' (within eight to ten years) (EAC Correspondence Log, 2022). The EAC have not identified any new comparative evidence relating to retreatment rates beyond 60 months. The EAC note that retreatment rates for GreenLight and TURP have been derived from the GOLIATH trial (Thomas *et al.* 2016), which reported retreatment rates up to five years; retreatment rates for HoLEP were an assumption derived from opinion from Clinical experts. The EAC notes that five of seven Clinical experts reported HoLEP as having the lowest reintervention rates across all interventions and did not suggest altering this rate (EAC Correspondence Log, 2022). The Company model used a 4-year time horizon for consistency with the model submitted for Rezum (MTG49), which only had 4-year follow-up data available. The EAC notes that 5-year follow-up data are available for GreenLight. The EAC notes that retreatment beyond this timeframe may not be captured within the model. The model is from a UK perspective, with a discount rate of 3.5% applied.

The Company noted that the same assumptions underpinning the original Rezum economic model submitted to NICE (within MTG49) were applied in the updated model for GreenLight, Table 21. As reported in the original Rezum assessment (Rezum EAC Assessment Report, 2019), for each comparator the simulated cohort undergoes an initial surgical procedure modelled as one-cycle tunnel state, where they are subject to costs associated with the procedure as well as short term adverse events (AEs). These are AUR ([acute urinary retention] non-serious and serious), UTI (non-serious and serious), bleeding (non-serious and serious), bladder contracture or stricture (serious), and transurethral resection (TUR) syndrome (serious). Two permanent AEs inform the long-term heath states of the model. These are erectile dysfunction (ED) and urinary incontinence; additionally there is a health state for concomitant ED and incontinence. Following treatment, patients may require surgical retreatment for recurrence of LUTS; repeat

surgery is represented by a tunnel state. Patients with urinary incontinence are assumed to be contraindicated for further surgery. The Company stated that ED was not considered within the updated Markov model base case as this outcome was more relevant when comparing minimally invasive procedures (EAC Correspondence Log, 2022). However, the Company included erectile dysfunction within scenario analysis, inputs were taken from a single source (Miner *et al.* 2006; which does not include GreenLight as an intervention) and was not adjusted between all patients and high-risk groups.. The Company also stated that patients with incontinence post-initial surgery are contraindicated for repeat surgery, and the risk of developing incontinence with revision surgery is assumed to be the same as for the initial procedure.

Figure 2: Structure of updated economic model.



Abbreviations: LT, long-term; ED, erectile dysfunction
*Surgical tunnel states include risk of short-term complications with surgery

Table 21. *Principal structural assumptions of the updated Markov model), with EAC summary of applicability to the updated model.*

Assumption	Company justification (from Rezum Assessment Report, 2019)	Company source	EAC opinion (for example relevance to GreenLight assessment, and whether changes have been applied)
All short-term complications with surgery are assumed to be independent and non-mutually exclusive.	This assumption is consistent with data reported in clinical trials.	Trial and HTA evidence (Roehrborn *et al.*, 2013, McVary *et al.*, 2016c, Lourenco *et al.*, 2008, Bachmann *et al.*, 2014)	Includes acute bleeding and urinary retention, and readmission for bladder neck contracture or stricture (Table 3 Company updated model submission). The sources for short-term complications were taken from an unpublished systematic review submitted by the Company with the Clinical Submission. The systematic review did not explicitly report which studies contributed to each outcome, therefore the EAC was unable to verify the model input parameters.
Only short-term complications commonly reported to be associated with BPH surgery that required medical interventions were considered in the model. This assumption meant that some severe events reported in the pivotal trials for Rezum and UroLift were not captured in the model. The Rezum pivotal trial reported two severe device- related adverse events that were not captured in the model: 1 case of nausea, requiring hospital admission and 1 case of urosepsis. Similarly, the LIFT study reported two severe adverse events related to the procedure that were not captured in the model: 1 case of clot retention and 1 subject who required removal of a bladder stone at 12 months.	The inclusion of these events was discussed with clinicians consulted during model development who provided feedback that such events are not common to BPH surgery and were likely to be one-off events. Furthermore, the impact of including these in the model was expected to be very low as the rates would have been <1% for each adverse event type.	Trial evidence (Roehrborn *et al.*, 2013, Roehrborn *et al.*, 2017c, McVary *et al.*, 2016c)	This assumption is not explicitly stated within the updated Company Economic Submission, however the EAC note that no GreenLight device-related adverse events are considered within the model. The EAC identified two studies reported technical failures with GreenLight (Trujillo *et al.* 2021, Rajih *et al.* 2017). Trujillo *et al.* (2021) reported intraoperative conversion to TURP in all 3 of 587 (0.5%) cases, whilst Rajih *et al.* (2017) reported malfunction of the MoXy fibre in 3 of 941 (0.3%) of patients. The EAC search of the MAUDE database noted 2 of 2,315 (0.1%) complications relating to GreenLight were classed as moderate complication or requiring minor intervention. The EAC consider the modelling of technical failures resulting in conversion to TURP in scenario analysis. Two Clinical experts estimated conversion rates were between 1 in 400 (0.25%) and 1 in 500 (0.2%), another Clinical expert estimated this would be less than 10%, and two other experts noted retreatments of this type are rare with one estimating rates lower than 1% (EAC Correspondence Log, 2022). A sixth Clinical expert noted that conversion from GreenLight to TURP intraoperatively is very rare with an experienced user with a possibility of higher incidence during the early learning curve with the technology (EAC Correspondence Log, 2022). The EAC will consider conversion within sensitivity analysis. The updated model includes costs of treating short-term adverse events only. A full description of AEs associated with GreenLight, including device related AEs, is discussed in Section 6.
While most short-term complications occur within 90 days of surgery, some short-term complications are reported up to 6 months post-surgery. Data on adverse events was therefore extracted from clinical trials up to 6 months post-surgery and where complications occurred between 3-6 months post-surgery, they are assumed to occur by 3 months for accounting purposes.	This assumption was applied to replicate the Markov structure applied in prior BPH models (Lourenco *et al.* 2008) and account for the fact that most short-term complications are resolved within 90 days of surgery.	Not applicable	This assumption is not explicitly stated within the updated Company Economic Submission although remains in the assumptions tab within the submitted model. The EAC note that the Company specify "the same assumptions underpinning the model submitted to NICE (MTG 49) were applied" within the updated Economic submission. The sources for short-term complications were taken from an unpublished systematic review, which reported non-severe complications within 3 months, and severe complications between 3 and 12 months. Given that the cycle length is 3 months it is unclear to the EAC how severe complications have been incorporated into the updated model.
Adverse events were categorised by two levels of severity namely non-severe and severe, where non-severe adverse events were assumed to be treated in primary care. Non-severe events were defined as non-acute, non-severe or ≤ grade 2 and included urinary retention, urinary tract infection and bleeding.	Complications were stratified by severity as non-severe events are expected to incur substantially lower costs. This assumption is consistent with the resource use assumptions applied in the GreenLight MTEP model (NICE MTG 29) and was validated with clinical experts consulted during model development.	NICE MTG29 (NICE, 2016). Clinical experts	The updated model includes values for non-severe and severe adverse events. The premise of classifying AEs as non-serious and serious is justifiable. In the GOLIATH trial (Bachmann *et al.* 2014), the Clavien-Dindo grade (Dindo *et al.* 2004) was used to inform AE severity for GreenLight and TURP. Severe adverse events were not explicitly reported in the updated submission, but were deduced from the model as acute urinary retention, bladder neck contracture or stricture, bleeding or blood transfusion, transurethral resection syndrome, urinary tract infection.

Assumption	Company justification (from Rezum Assessment Report, 2019)	Company source	EAC opinion (for example relevance to GreenLight assessment, and whether changes have been applied)
Adverse events with TURP and HoLEP were sourced from Lourenco *et al.* (2008), however this meta-analysis did not report adverse events by severity. The following assumptions were therefore applied to calculate the rates of severe and non-severe events for Mono-TURP, Bi-TURP and HoLEP: 1. 90% of UTI events were assumed to be non-severe. 2. The distribution of severe and non-severe urinary retention events was sourced from the TURP arm of GOLIATH RCT (Backmann *et al.* 2014). 3. All bleeding, bladder neck contracture / stricture / bladder stones and transurethral resection syndrome (TUR) events reported in Lourenco *et al.* (2008) were assumed to be severe.	Lourenco *et al.* (2008) reported results from a meta-analysis previously used to inform NICE guidance. 1. Clinical experts consulted during model development. They provided feedback that the majority (estimated ~90%) of urinary tract infections after surgery were non-severe and could be treated at home / primary care with medication. 2. The GreenLight RCT reported the rates of urinary retention for TURP by grade. 3. Clinical experts provided feedback that bleeding events occurring with TURP are expected to be grade 3+ and that all stricture / TURs events are treated in secondary care.	HTA and trial evidence (Lourenco *et al.*, 2008, Bachmann *et al.*, 2014) and Clinical Expert Opinion.	The updated model uses values from Lourenco *et al.* (2008); Bachmann *et al.* (2014) in addition to the unpublished systematic review submitted by the company as part of the Clinical Submission. A hybrid method of estimating AEs for GreenLight, TURP, and HoLEP, using meta-analysis and RCT data, was appropriate, but introduced some uncertainty into the model. The inclusion of additional sources of information, without explicit reporting of primary sources, introduces further uncertainty into the model. The EAC consider the modelling and inputs for AEs for high-risk patients as not appropriate or robust. Due to the lack of new randomised comparative evidence, clinical parameters for AEs will not be updated in the EAC base case and the EAC accepts this assumption for all patients.
All incontinence events were assumed to be moderate / severe and permanent.	This replicates the assumption applied in Lourenco *et al.* (2008). The same assumption was applied and accepted in the Neotract MTEP submission for UroLift (NICE, 2015d).	HTA (Lourenco *et al.*, 2008) NICE MTG26 (NICE, 2015d)	Whilst not explicitly stated within the updated submission, the EAC identify that the updated model used costs associated with incontinence from NICE MTG26. The risk of permanent incontinence was a feature of the meta-analysis and economic model of the HTA (Lourenco *et al.*, 2008), and this assumption was accepted for NICE MTG26 (NICE, 2015d). Based on precedent, the EAC accepts this assumption.
Patients that have incontinence after the initial procedure remain in the same health state and cannot have repeat surgery for LUTS.	This replicates the assumption applied in Lourenco *et al.* (2008), justified because permanent incontinence is contraindicated for further surgical treatments	HTA (Lourenco *et al.*, 2008)	Unchanged from Rezum model, Page 4 updated Company Economic Submission. Permanent incontinence being a contraindication for further surgery for LUTS was a feature of the meta-analysis and economic model of the HTA (Lourenco *et al.* 2008). Based on this precedent, the EAC accepts this assumption.
The risk of incontinence was incorporated for GreenLight, TURP and HoLEP.	Risk of incontinence of GreenLight has been taken from the GOLIATH study (Bachmann *et al.* 2013), whilst the risk of incontinence for monopolar and bipolar TURP, and HoLEP was taken from a systematic review by Lourenco *et al.* (2008).	Trial data (Roehrborn *et al.*, 2013, Roehrborn *et al.*, 2017c, McVary *et al.*, 2016a, Bachmann *et al*, 2013, Lourenco *et al.* 2008)	Unchanged from Rezum model.
All revision surgeries after TURP are repeated with TURP.	This assumption is consistent with clinical opinion.	NICE MTG29 (NICE, 2016). Clinical experts	Within the updated GreenLight model the Company have assumed that 100% of surgical retreatments for patients receiving TURP will undergo further TURP surgery. Two Clinical experts advised that these figures were in line with their experience (EAC Correspondence Log, 2022). One expert stated that for those undergoing TURP as the initial procedure 20% would undergo GreenLight, 80% TURP as retreatment. Another expert noted that a proportion of patients (estimated at 1 in 30 or 40) would undergo HoLEP retreatment following TURP or GreenLight, whilst another expert noted that 100% retreatment of TURP following TURP was too high, although did not propose an alternative. Two experts were unsure of proportions and unable to provide comment (EAC Correspondence Log, 2022).

Assumption	Company justification (from Rezum Assessment Report, 2019)	Company source	EAC opinion (for example relevance to GreenLight assessment, and whether changes have been applied)
50% of revision surgeries after Rezum or GreenLight are repeated with TURP. Where symptoms return after an initial Rezum or GreenLight procedure, patients may opt to have the same index surgery or have a TURP.	A 50% split between TURP and the index surgery was assumed because clinical opinion suggests that this decision is likely to vary by hospital	Assumption informed by Clinical expert opinion.	Within the updated GreenLight model, the Company have assumed that 50% of patients receiving GreenLight requiring surgical retreatment, and 0% of patients receiving HoLEP requiring surgical retreatment will undergo TURP. The company do not provide any source information for the retreatment of patients receiving TURP, the proportions for patients receiving GreenLight or HoLEP are informed by assumptions provided by clinical experts consulted during model development. The Company have adjusted the retreatment rates when modelling a high-risk population, but have not adjusted the proportion undergoing retreatment with TURP. Two Clinical experts advised that these assumptions were appropriate, one expert stated that all retreatments conducted after GreenLight would be TURP. Another expert advised for GreenLight 75% would undergo GreenLight and 25% TURP. Another expert stated that HoLEP may be used in some patients requiring surgical retreatment following TURP. Two experts were unsure of proportions and unable to provide comment (EAC Correspondence Log, 2022).
No revision surgeries occur with HoLEP	HoLEP is an ablative procedure therefore a repeat procedure is not appropriate as all tissue has already been removed	Clinical Expert Opinion	This assumption has been applied in the updated model. Clinical experts unanimously agreed that there was the potential for surgical retreatment (for example, when not all of the prostate is enucleated) on rare cases following HoLEP, however as this could not be quantified, but was definitely considered to be rare (Rezum Assessment Report, 2019), and therefore this assumption was considered appropriate. The Company have included a retreatment rate of 14.6% at 5.2 years in high-risk patients receiving HoLEP within their economic model; as derived from the unpublished systematic review. The primary sources for these figures were not explicitly reported for the EAC to verify. Four of seven Clinical experts suggest that HoLEP has the lowest retreatment rates and were unsure why this would be the highest value in high-risk patients (EAC Correspondence Log, 2022).
Mortality is excluded from the model.	Prior economic models (NICE, 2016, NICE, 2015d, Lourenco *et al.*, 2008) did not include mortality due to limited evidence suggesting treatments for BPH influences overall survival. Hence, due to the short time horizon of the model, mortality was excluded from the model.	Not applicable	The EAC agrees mortality is not relevant to the model and remains unchanged in the updated submission.
The risk of developing incontinence or ED with repeat surgery is assumed to be the same as the initial procedure.	There is no data reporting these outcomes in repeat surgery or suggest that these rates differ.	Not applicable	This remains unchanged in the updated submission. The EAC accepts there is no data to inform this transition probability. There is also a lack of data to support the continued efficacy of repeat procedures.

Abbreviations: ED, erectile dysfunction; HES, hospital episodes statistics; HoLEP, holmium laser enucleation of prostate; TURP, transverse resection of prostate.

Population

The Company have stated that the Markov model (original developed for Rezum MTG49) was adapted to enable modelling a scenario including high-risk patients only. This approach was not applied in the Rezum economic model as Rezum is a minimally invasive intervention. The updated Economic Submission does not explicitly state the definition of a high-risk population, however as data to populate the high-risk scenario was derived from the referenced unpublished systematic review, the EAC assumes that "high-risk" includes patients:

- with large prostates (greater than or equal to 80 ml),
- taking antithrombotic agents,
- with urinary retention,
- aged over 80 years,
- with significant comorbidity (not explicitly specified).

The EAC note that the definition of high-risk included in the unpublished systematic review differ from that defined in the final scope (NICE MT564 Final Scope, 2021).

Intervention

The Markov model was updated to focus on GreenLight XPS 180 W as the main intervention; the EAC notes that the main intervention and comparators are adjustable via model settings.

Comparators

Whilst the updated model included capability to compare GreenLight to Rezum and UroLift, settings were restricted to compare withonly TURP and HoLEP in line with the final scope (NICE MT564 Final Scope, 2021). The model reports only aggregated results for TURP assuming 25% mono-polar and 75% bipolar (which is in line with the EAC base case for Rezum).

Outcomes

Procedural related resource included duration of operation, and length of hospital stay. The EAC notes that pre-operative consultation and follow-up consultation also contributed to procedural costs, but were applied equally across all arms. Efficacy outcomes included surgical retreatment at follow-up, and the proportion retreated with TURP. Short-term complications were categorised as either non-severe (non-acute urinary retention, non-serious urinary tract infection, and non-acute bleeding) or severe (acute urine retention, bladder neck contracture or stricture, bleeding or need for blood transfusion, transurethral resection syndrome and urinary tract infection). Long-term complications included incontinence only (erectile dysfunction was not included in the updated base case but was included as a scenario).

Economic model parameters

Clinical parameters and variables

Clinical parameters were unchanged from the Rezum model when modelling all patients, Table 22. However, some clinical parameters (surgical retreatment, non-acute urine retention, acute urine retention, bladder neck contracture or stricture, bleeding or need for blood transfusion, length of hospital stay) were changed when modelling the high-risk population, Table 22, using results from an unpublished systematic review submitted by the Company as part of their Clinical Submission. The Company have confirmed that the systematic review has been resubmitted for publication with updated searches, and remains unpublished as of 20/04/2022 (EAC Correspondence Log, 2022). This systematic review reported outcomes from more than 100 studies, which included GreenLight XPS as well as other BPH surgical interventions. There was some ambiguity regarding the inclusion and exclusion criteria for studies, which the Company highlighted at fact-check. The EAC was unable to verify the application of the inclusion and exclusion criteria as the input source for each outcome was not explicitly reported and note that some studies were included on the basis of mean values of a mixed population (Table S4). The EAC critically appraised the unpublished systematic review, Appendix B4. Updated clinical parameters were taken from the Company submitted systematic review; however, as the systematic review

did not explicitly report which studies contributed to each outcome, the EAC was unable to verify the model input parameters.

The systematic review missed a number of eligible studies (identified by the EAC during its independent literature review, Table_B4.3) which included high-risk patients. The systematic review:

- included conference abstracts (lacking peer-review);
- had ambiguity in the inclusion and exclusion criteria and how this was applied in practice; was not transparently reported such that the EAC was unable to verify outcomes;
- some model inputs (for example, retreatment rates) lacked clinical validity as highlighted by the Clinical experts (EAC Correspondence Log, 2022);
- acknowledged large heterogeneity across included studies preventing meta-analysis;
- was funded by Boston Scientific;
- declared conflicts of interest as 3 authors being employees of Boston Scientific, 2 receiving funding from Boston Scientific to conduct the research, 3 worked as a consultant for Boston Scientific.

Therefore, the EAC would consider the unpublished systematic review as low quality and the results as not robust. No new published literature relevant to the scope was identified in the latest Economic Submission.

The EAC note that the most robust comparative evidence to date (GOLIATH trial) used for the GreenLight economic modelling included patients with prostates over 100 ml and patients with increased risk of bleeding with outcomes not reported exclusively. This trial data is used in the original and updated GreenLight economic modelling. The EAC have identified 58 new studies within this Guidance Update, of which 50 studies include high-risk patients and the EAC have identified only 2 comparative studies conducted

exclusively in high-risk patients or including reporting of high-risk subgroups (Mesnard *et al.* 2021, Gondran-Tellier *et al.* 2021). The non-randomised study by Mesnard *et al.* (2021), conducted exclusively in patients with haemophilia, reported on outcomes in patients receiving GreenLight (n=5) compared with patients receiving TURP (n=5). Blood loss and length of stay were greater in patients receiving TURP, although no statistical analysis was performed due to a small sample size. No intraoperative complications were identified in either group. Three patients presented with complications following hospital discharge after GreenLight, two of which required readmission, including one undergoing surgical revision. One patient also took anticoagulant medication, although it was unclear which intervention arm this patient was allocated to due to poor reporting. The non-randomised study by Gondran-Tellier *et al.* (2021) compared outcomes with GreenLight (n=62), TURP (n=48), enucleation (GreenLEP or HoLEP, n=21), prostate artery embolism (n=15) and open prostatectomy (n=25) in 171 patients with urinary retention. One patient receiving TURP and one patient receiving GreenLight required reoperation within 12 months after the original procedure with the secondary procedure not specified. The study also included some patients taking antithrombotic medication or with prostate volumes over 100 ml. Median lengths of stays for patients receiving TURP and GreenLight in both studies were greater than five days, which are not supported by the opinion from Clinical experts (EAC Correspondence Log, 2022), BAUS Bladder Outflow Obstruction audit, 2019, Hospital Episode Statistics data or other published evidence (Table 11). Neither study reported on procedure duration. Both studies were conducted in France, and therefore may lack generalisablility to the UK NHS setting.

The EAC consider there to be insufficient robust evidence to support economic modelling specifically for high-risk populations. Modelling all high-risk patients collectively (for example, prostates larger than 100 ml, increased risks of bleeding, urinary retention) may not be appropriate or generalisable. For example, there was consensus from the Clinical experts that procedure length is most affected by prostate size, whilst urinary retention may not be considered as a high risk factor (EAC Correspondence Log, 2022). One

Clinical expert suggested that nearly 50% of patients having surgery for BPH have urinary retention, and according to the BAUS Bladder Outflow Obstruction Audit (2019), the indication for surgery in 43% was acute or chronic urinary retention (EAC Correspondence Log, 2022). The study by Gondran-Tellier *et al.* (2021) conducted exclusively in patients with urinary retention also included patients with prostate volumes over 100 ml or taking antithrombotic medication, however did not report outcomes exclusively for these other risk factors. There is a lack of comparative, randomised evidence in each high-risk group to support economic modelling for independent risk factors.

The EAC would consider that modelling all-patients, the approach used in the original Rezum model, as more appropriate and more generalisable to UK NHS patients.

Table 22: Clinical parameters used in the updated Company Markov economic model

Parameter	All patients *[Settings!X21=No]*				EAC comment on "all patients"	High-risk only *[Settings!X21=Yes]*				EAC comment on "high-risk" subgroup
	GreenLight	**mTURP**	**bTURP**	**HoLEP**		**GreenLight**	**mTURP**	**bTURP**	**HoLEP**	
Proportion required surgical retreatment at follow-up	6.9%, 5.0 years	5.8%, 5.0 years	5.8% , 5.0 years	0.0%, 5.2 years	The proportion of retreatment for GreenLight has been updated from the Rezum model (5.8%, 5 years) based on MTG49 and data from the GOLIATH study (Thomas *et al.* 2016) that found an 18% increase in retreatment with GreenLight than TURP) Due to the lack of new randomised comparative evidence and long-term follow up, the EAC consider the GOLIATH study remains the most robust source of retreatment when the model is not restricted to high-risk patients only. Three Clinical experts also stated that the retreatment rate estimations for all patients were reasonable and in line with clinical practice (EAC Correspondence Log, 2022).	5.95%, 5.0 years [N=5 studies, range: 0% to 11.9%]	12.5%, 5.0 years [N=4 studies, range: 0% to 25%]	3.7%, 5.0 years [N=2 studies, range: 2.9% to 4.5%]	14.6%, 5.2 years [N=6 studies; range: 0% to 29.2%]	Midpoint between the range as reported in the unpublished systematic review (Table S12, page 75) submitted by the Company. The unpublished systematic review does not explicitly report which studies were used, therefore the EAC is unable to verify the proportion of patients requiring surgical retreatment during follow-up. One Clinical expert stated that the proportions in the "high-risk" population do not make sense clinically (EAC Correspondence Log, 2022). The expert stated that it was not clear why reintervention rate would be the highest for HoLEP in a high-risk population, as it would be expected to have the lowest (EAC Correspondence Log, 2022). Another Clinical expert noted that retreatment rates for HoLEP should be the same in both groups and agreed with three other experts that HoLEP would have the lowest reintervention rate across all groups (EAC Correspondence Log, 2022). Three Clinical experts also queried the large difference in retreatment between mono- and bi-polar TURP arms in a high risk population, noting these would be anticipated to be the same (EAC Correspondence Log, 2022). Two Clinical experts consider the Company estimations to be appropriate, while another commented that it was difficult to comment due to poor data (EAC Correspondence Log, 2022). Due to the risk of bias in the unpublished systematic review, the EAC would consider these estimates of retreatment in the high-risk population as not robust. From the literature identified by the EAC, reintervention rates ranged from 0 to 15.2% following GreenLight PVP. Only one study (Gondran-Tellier *et al.* 2021) conducted exclusively in a high-risk population (all with urinary retention, 47% on antithrombotic, prostate volume IQR 56-110 cm^3) reported that 5 of 171 (2.9%) patients required reoperation within 12 months with 1 patient in both TURP and GreenLight arms.
Proportion retreated with TURP	50%	100%	100%	0%	MTG49, 2019	50%	100%	100%	0%	No change in high-risk subgroup. One Clinical expert stated that they would use TURP for all retreatments following an initial GreenLight procedure (EAC Correspondence Log, 2022). One Clinical expert stated that they may use HoLEP in some patients requiring retreatment after an initial GreenLight or TURP procedure. There is a lack of available data to quantify the proportion this occurs. Additionally, the EAC was unable to alter the structure of the updated GreenLight economic model to account for this. Therefore, total costs of GreenLight and TURP in the economic model are likely an underestimate.
Non-severe adverse event										

- Non-acute UR	5.9%	1.2%	2.0%	0.8%	MTG49, 2019	8.35% [mid-point between 0% and 16.7%]	0.75% [mid-point between 0% and 1.5%]	0.75% [mid-point between 0% and 1.5%]	10.4% [mid-point between 0.6% and 20.2%]	Company reports that this combines rate for any urinary retention, assuming rates between 1 and 3 months and 3 to 12 months are mutually exclusive as reported in the unpublished systematic review (Table S13, page 77). The EAC notes that 8.35% urine retention in the GreenLight arm represents the mid-point between the upper estimates of the proportion affected with urine retention (10.8% with urine retention between 1 to 3 months obtained from 3 studies combined and 5.9% with urine retention between 3 and 12 months obtained from 3 studies) and the lower estimates (0% between 1 and 3 months, and 0% between 3 and 12 months). The number of studies reporting the outcomes (retention between 1 and 3 months, and between 3 and 12 months) is different across comparators The EAC notes that from the unpublished systematic review that only 2 studies reported on urine retention between 3 and 12 months in the mono-TURP arm (between 0 and 1.5%); none reported on urine retention between 1 and 3 months, and none reported on bi-TURP.. Due to the risk of bias in the unpublished systematic review, the EAC would consider these estimates of non-acute urinary retention in the high-risk population as not robust.
- Non-serious UTI	19.1%	5.4%	5.4%	5.3%	MTG49, 2019	19.1%	5.4%	5.4%	5.3%	No change in high risk subgroup
- Non-acute bleeding	8.8%	0.0%	0.0%	0.0%	MTG49, 2019	8.8%	0.0%	0.0%	0.0%	No change in high risk subgroup
Severe adverse event risks										
- Acute urinary retention	6.6%	3.8%	6.6%	2.7%	MTG49, 2019	3.2% [N=1 study reported readmission for urinary retention between 3 and 12 months]	3.8%	6.6%	2.7%	Acute urine retention was only updated in the model for the GreenLight arm. The Company has stated that only 1 study reported on readmission for urinary retention affected between 3 to 12 months, which included 374 GreenLight patients (3.2%). According to Table S13 of the unpublished systematic review, no studies reported on this outcome for the TURP or HoLEP comparator arms, therefore it is unclear why these outcomes have not changed in the high-risk model. Due to the risk of bias in the unpublished systematic review, the EAC would consider these estimates of acute urinary retention in the high-risk population as not robust.
- Bladder neck contracture or stricture	4.4%	7.0%	9.7%	5.9%	MTG49, 2019	0.45% [mid-point between 0% and 0.9%]	7.1% [mid-point between 4.1% and 10.1%]	7.15% [mid-point between 4.4% and 9.9%]	4.5% [mid-point between 0% and 9%]	Company reports this is a sum of rates of readmission for bladder neck constracture and stricture (assuming events are mutually exclusive) as reported in the unpublished systematic review (Table S12, page 75) submitted by the Company. The number of studies reporting the outcomes (reintervention for urethral stricture, and reintervention for bladder neck contracture) is different between the different outcomes. The unpublished systematic review does not explicitly report which studies were used, therefore the EAC is unable to verify the proportion of patients experiencing this adverse event. Due to the risk of bias in the unpublished systematic review, the EAC would consider these estimates of bladder neck contracture or stricture in the high-risk population as not robust.

- Bleeding or blood transfusion	2.9%	8.0%	8.2%	2.2%	MTG49, 2019	15.45% [mid-point between 2.6% and 28.3%]	11.15% [mid-point between 0% and 22.3%]	20.95% [mid-point between 2.8% and 39.1%]	19.75% [mid-point between 0% and 39.5%]	Company reports this is a sum of rates of blood transfusion, reintervention for clot and reintervention for haematuria (assuming events are mutally exclusive) as reported in the unpublished systematic review (Table S11, page 74) submitted by the Company. The number of studies reporting the outcomes (blood transfusion, reintervention for clot retention and reintervention for haematuria) is different between the different comparators. The unpublished systematic review does not explicitly report which studies were used, therefore the EAC is unable to verify the proportion of patients bleeding or requiring blood transfusion. Due to the risk of bias in the unpublished systematic review, the EAC would consider these estimates of bleeding in the high-risk population as not robust. From the literature identified by the EAC bleeding rates requiring blood transfusion ranged from 0 to 2.2% when measured intraoperatively and 0.6 to 0.8% when measured within 30 days post-operatively, Table 14. • Goueli *et al.* (2017) reported higher blood transfusion rates in patients with urinary retention with 2 of 137 patients (1.5%) compared to 0 of 198 patients (0%) without urinary retention. • Campobasso *et al.* (2020) noted higher rates for blood transfusion in patients in patients with prostates smaller than 100 ml with 6 of 916 (0.7%) compared with patients with prostates larger or equal to 100 ml with 0 of 115 (0%). • Mattevi *et al.* (2020) noted no cases of blood transfusions in patients receiving GreenLight compared with 4 of 50 (8%) patients receiving TURP.
- Transurethral resection syndrome	0.0%	3.0%	0.5%	0.9%	MTG49, 2019	0.0%	3.0%	0.5%	0.9%	No change in high-risk subgroup. One Clinical experts stated that TUR syndrome may be higher in patietns with larger prostates, and mainly with mono-polar TURP (less common with other modalities).
- Urinary tract infection	0.0%	0.6%	0.6%	0.6%	MTG49, 2019	0.0%	0.6%	0.6%	0.6%	No change in high-risk subgroup
Long-term incontinence	1.1%	3.0%	1.8%	2.9%	MTG49, 2019	1.1%	3.0%	1.8%	2.9%	No change in high-risk subgroup. One Clinical expert stated that incontinence rates are known to be higher in HoLEP with large prostates (for example greater than 150g).
Duration of operation	49.6 mins	66.0 mins	66.0 mins	80.2 mins	Three Clinical experts stated that the procedure durations seemed reasonable (one expert only had experience with GreenLight and mono-polar TURP).	49.6 mins	66.0 mins	66.0 mins	80.2 mins	No change in high-risk subgroup. Two Clinical experts advised that BPH surgery would not take longer in patients at risk of bleeding or those with urine retention, but would be longer depending on size of prostate (EAC Correspondence Log, 2022). One Clinical expert also advised that HoLEP operating time can vary considerably (from 45 minutes to 2 to 3 hours) depending on prostate size, and would increase conducted during training list (which is likely due to HoLEP requiring considerably more training than other BPH surgeries). The EAC has increased HoLEP procedural duration within sensitivity analysis.

Length of stay	0.70 days	3.03 days	2.33 days	2.0 days	Unchanged from Rezum model Five Clinical experts stated that these estimates were reasonable (EAC Correspondence Log, 2022). Three Clinical experts noted that HoLEP length of stay would be 0 to 1 days, one also commented the length of stay for mTURP and bTURP is high, suggestion 2, and 1.5 to 2 days respectively (EAC Correspondence Log, 2022).	2.95 days [N=18 studies, mean: 0.9 to 5.0; median: 0.8 to 4.0]	6.85 days [N=20 studies; mean: 2.2 to 11.5; median: 2.0 to 6.0]	6.80 days [N=16 studies; mean: 1.1 to 12.5 days; median: 3.0 to 4.0]	3.2 days [N=42 studies; mean: 0.8 to 5.5; median: 1 to 6]	Midpoint between the highest and lowest *mean* as reported in the unpublished systematic review (Table S10, page 48) submitted by the Company. The EAC notes that if the Company used the midpoint between the highest and lowest *median* that the LoS would have been lower for all arms with the exception of HoLEP. The systematic review does not explicitly state which studies were used, and therefore the EAC is unable to verify the LoS for any arm. Due to the risk of bias in the unpublished systematic review, the EAC would consider these estimates of length of stay in the high-risk population as not robust. One Clinical expert stated that patients classified as high-risk due to urinary retention would not normally have a higher length of stay (EAC Correspondence Log, 2022). There is a lack of consensus from the Clinical experts regarding how length of stay parameters would be adjusted specifically for high-risk patients, for example, one expert noted “I think it is impossible to assess since not all high risk patients are equal in terms of length of stay”. There was also inconsistent responses where 3 experts agreed with the Company estimates for LoS in high-risk patients, 3 said that the estimates were too long, and one was unsure and commented that TURP would not be used in high-risk patients (EAC Correspondence Log, 2022). One Clinical expert referenced the BAUS Bladder Outflow Obstruction audit, 2019 which included 1,456 cases (which comprised 37.7% bipolar TURP, 22.8% monopolar TURP, 10.2% HoLEP, 7.4% UroLift, 6.1% GreenLight, 4.8% Rezum, 4.7% BNI/TUIP, 4.2% prostatic artery embolisation, 0.1% open prostatectomy, 1.9% other) and reported a median length of stay of 1 day across all cases.
Pre-operative consultation (per patient)	1.0	1.0	1.0	1.0	Unchanged from Rezum model	1.0	1.0	1.0	1.0	No change in high risk subgroup
Follow-up consultation (per patient)	1.0	1.0	1.0	1.0	Unchanged from Rezum model	1.0	1.0	1.0	1.0	No change in high risk subgroup
Abbreviations: BAUS, the British Association of Urological Surgeons; BNI, bladder neck incision; EAC, external assessment centre; TUIP, transurethral incision of the prostate; TURP; transurethral resection of prostate; UR, urine retention; UTI, urinary tract infection										

Resource identification, measurement and valuation

The updated Company Economic Submission includes costs associated with device, theatre, hospital stay, pre and post testing, treating short-term adverse events, incontinence, repeat surgery and short-term complications, and repeat surgery for incontinence treatment, Table 23. The updated Company Markov model reports costs in 2019 GBP and does not explicitly report the source of each cost. The EAC considered that sourcing all costs from MTG49, 2019 as appropriate and consistent across all arms.

Table 23: Cost parameters used in the updated Company Markov economic model

Costs	Updated model (2021)	EAC comment
GreenLight total - GreenLight XPS fibre	**£550** £550	Company reports this as the average list price in the UK. The majority of costs have come from the original Rezum assessment (EAC Assessment Report, 2019), with the exception of the cost of GreenLight which was previously £540. The EAC would recommend using all costs from the same source for consistency. Cost does not include saline for cooling the laser, however its inclusion would have limited impact on total costs.
Mono-TURP total - Mono-loop (x1) - Glycine fluid (x4) - Roller ball piece (x0.5) - Ellik evacuator (x1) - Saline bladder irrigation (x8.93; 7 units, for 2.55 days, in 50% of cases)	**£165.35** £52.60 £21.37 £25.00 £21.04 £45.34	Company references MTG29 inflated using CPI. Costs broadly agree with those calculated by EAC (see Table 18). Saline for bladder irrigation not initially included, however was added to the updated model following a query by the EAC to ensure consistency with the prior decision tree model (EAC Correspondence Log, 2022). Model assumes 25% mono-polar TURP which is in agreement with the EAC basecase of Rezum (MTG49, 2019), and in agreement with the Clinical experts experience (EAC Correspondence Log, 2022). One Clinical expert referenced the BAUS Bladder Outflow Obstruction audit, 2019 which included 332 cases of monopolar TURP and 548 cases of bipolar TURP (38% monopolar). The change in mono/bi-polar TURP will be addressed in sensitivity analysis.
Bi-TURP total - Bi-loop (x1) - Ellik evacuator (x1) - Saline bladder irrigation (x8.93; 7 units, for 2.55 days, in 50% of cases)	**£255.72** £189.34 £21.04 £45.34	Company references MTG29 inflated using CPI. Costs broadly agree with those calculated by EAC (see Table 18). Saline for bladder irrigation not initially included, however was added to the updated model following a query by the EAC to ensure consistency with the previous decision tree model (EAC Correspondence Log, 2022).
HoLEP total	**£448.83**	

Costs	Updated model (2021)	EAC comment
- Single use HoLEP fibre (x0.5) - Reusable HoLEP fibre (x0.02 – reusable used in 50% cases, reused 25 times) - Morcellator cutting blade (x1) - Suction tubing (x1) - Omni-jugs for collecting fluid (x0.17 – 1 used for 6 procedures) - Ellik evacuator for chip removal (x1) - Stripper and cleaver (x0.5, only for reusable) - HoLEP generator (1 used by 250 patients, 10 year lifetime) - HoLEP morcellator (1 used by 250 patients, 10 year lifetime)	£94.47 £14.73 £210.38 £21.04 £1.23 £21.04 £26.30 £36.82 £12.62	Company references MTG29 inflated using CPI. Costs broadly agree with those calculated by EAC (see Table 18); however, the EAC has stated that capital costs of the HoLEP generator and morcellator are not subject to discount as they arise in year 1 of the time horizon for each patient.
Cost of operating theatre (per min)	£13.37	MTG49, 2019
Cost of hospital bed day	£365.00	Same as EAC base case (MTG49, 2019) using weighted average of elective and non-elective bed days.
Pre-operative urologist consultation	£127	MTG49, 2019
Post-operative urologist consultation (follow-up)	£105	MTG49, 2019
Pre- and post-operative tests	£129	MTG49, 2019 (based on 100% patients undergoing ultrasound, 20% undergoing urodynamic test, 20% undergoing flexible cystoscopy)
Short-term non-severe adverse events - Non-acute UR - Non-serious UTI - Non-acute bleeding	 £40.61 £39.18 £38.29	MTG49, 2019
Short-term severe adverse events - Acute urinary retention - Bladder neck contracture/stricture - Bleeding/blood transfusion - Transurethral resection syndrome - Urinary tract infection	 £3,061.79 £330.00 £357.95 £2,102.00 £781.00	MTG49, 2019

Costs	Updated model (2021)	EAC comment
Long-term incontinence (annual)	£2,279.90	MTG49, 2019
Abbreviations: CPI, consumer price index; EAC, external assessment centre;		

Sensitivity analysis

Summarised results and sensitivity analyses were presented on separate worksheets within the updated Markov model excel spreadsheet, with tornado diagrams used to present univariate deterministic sensitivity analysis (DSA) and incremental cost difference curves for probabilistic sensitivity analysis (PSA). The Company have adopted the use of derived pseudo 95% confidence intervals, bounded by the low and high means obtained from the unpublished systematic review, to address the uncertainties around the parameters for high-risk patients. Duration of operation and length of stay were sampled from log normal distributions to account for variabilities associated with high-risk patients only.

The EAC would consider that the addition of the high-risk scenario has reduced the transparency of the economic model, and introduced errors into the model. The EAC also noted several discrepancies in the model resulting in the EAC being unable to replicate the PSA of the updated Company model, including:

- differences in the PSA parameters applied the updated Economic Submission and those applied in the updated model (for example, low and high values of non-acute urinary retention in GreenLight arm in “HighRisk data, UK” and “Sensitivity” worksheets),
- despite the clinical parameters when modelling all patients matching those of the original Rezum model, differences in PSA parameters were identified between the two (Appendix E3),
- PSA distribution errors identified in the original Rezum economic model (Appendix E of the Rezum Assessment Report, 2019) have been corrected in the updated model for mono-TURP, bi-TURP, and HoLEP arms, with errors remaining for GreenLight, when modelling all patients.

These discrepancies were highlighted to the Company (on 04/04/2022, EAC Correspondence Log, 2022) and the Company agreed that the PSA parameters noted by the EAC in the Rezum Assessment Report were more precise and recommended these to be corrected (EAC Correspondence Log, 2022).

The Company removed erectile dysfunction (ED) as an outcome, and provided justification of this approach as being due to the intervention (GreenLight) and comparators (HoLEP, TURP) all being invasive treatment options, and "not a relevant risk factor or may not have cost implications for all men". The EAC consider this approach to be justified. The Company subsequently added ED outcomes within scenario analysis. To incorporate this in the economic model the Company assumed that the probability of developing ED after primary GreenLight or HoLEP surgery, was equivalent to that of two other treatment options (2% in patients undergoing transurethral needle ablation or transurethral microwave thermotherapy) without providing explicit rationale. The EAC note that values within the scenario analysis are derived from a single source (Miner *et al.* 2006), which does not include GreenLight as an intervention and was published prior to GreenLight 180 W XPS being available. The EAC would consider this scenario analysis as not robust due to lack of available evidence.

9.5 *Results from the updated economic modelling*

EAC replication of the Company base case

The EAC altered the Company Markov model (removing cost of saline bladder irrigation and reducing the cost of GreenLight from £550 to £540) to replicate the results of the Rezum EAC base case model (MTG49, 2019) with GreenLight being cost-saving by £631 and £712 per patient over 4 years when compared with TURP and HoLEP respectively, Table 24. Inclusion of saline irrigation in both mono- and bi-TURP arms, and increasing GreenLight costs to £550 (in line with updated Company model), resulted in GreenLight remaining cost-saving by £718 and £700 per patient over 4 years when compared to TURP and HoLEP respectively.

The Company reported that cost savings in a high-risk population associated with GreenLight increased to £1,556 and £753 per patient over 4 years when compared with TURP and HoLEP respectively, Table 24. The Company Submission reported that savings associated with GreenLight in a high-risk population were between £306 and £2,785 per patient over 4 years when compared with TURP using the lowest and highest mean values of clinical parameters as derived from the unpublished systematic review. Similarly, cost savings associated with GreenLight were between £413 and £1,185 per patient over 4 years when compared with HoLEP using the

lowest and highest mean values of clinical parameters. The EAC was unable to run the Company model (version 2) with these parameters to derive these values independently. The EAC made a number of changes to the updated Company GreenLight model, with the majority of scenarios demonstrating GreenLight to be cost-saving when compared with both TURP and HoLEP at 4 years, Table 25. Cost savings associated with GreenLight were reduced when the procedural duration of TURP was changed to be the same as GreenLight. Additionally, GreenLight became cost-incurring when the HoLEP procedural duration was reduced to 60 minutes.

Table 24: Results of the updated Company Markov model (high-risk population and all patients)

Cost breakdown	Cost per patient (£), after 4 years - All patients - GreenLight reduced to £540 - Saline bladder irrigation removed from TURP			Cost per patient (£), after 4 years (all patients)			Cost per patient (£), after 4 years (high-risk only)		
	GreenLight	TURP	HoLEP	GreenLight	TURP	HoLEP	GreenLight	TURP	HoLEP
Device Cost	540.00	187.79	448.83	550.00	233.13	448.83	550.00	233.13	448.83
Theatre Costs	663.15	882.42	1,072.14	663.15	882.42	1,072.14	663.15	882.42	1,072.14
Cost of Hospital Stay	255.50	914.33	722.70	255.50	914.33	722.70	1,076.75	2,486.56	1,149.75
Cost of pre and post tests	490.40	490.40	490.40	490.40	490.40	490.40	490.40	490.40	490.40
Cost of treating short-term adverse events	240.96	271.23	137.29	240.96	271.23	137.29	169.02	301.63	199.59
Cost of treating incontinence	92.42	174.54	244.49	92.42	174.54	244.49	92.42	174.54	244.49
Repeat surgery and short-term complications	118.29	110.44	0.00	119.61	112.26	0.00	151.51	178.92	332.64
Cost of treating repeat incontinence*	2.83	3.10	0.00	2.83	3.10	0.00	2.43	3.72	10.82
Total Costs	**2,403.55**	**3,034.25**	**3,115.85**	**2,414.88**	**3,081.41**	**3,115.85**	**3,195.69**	**4,751.32**	**3,948.66**
Net diff vs GreenLight	**-**	**-630.70**	**-712.30**	**-**	**-666.54**	**-700.97**	**-**	**-1,555.63**	**-752.96**

Abbreviations: HoLEP, holmium laser enucleation of the prostate; TURP, transurethral resection of the urethra.
* Incontinence caused by repeat surgery. Green indicates GreenLight is cost-saving; Red indicates GreenLight is cost-expending.

Table 25: EAC univariate changes to the Company updated Markov model (version 2)

Scenario	Mean discounted cost per patient (£), after 4 years (results from updated Company model			Cost difference (GreenLight-Comparator)		EAC Comment [Economic model setting changes]
	GreenLight	TURP	HoLEP	TURP	HoLEP	
Basecase (all)	£2,414.88	£3,081.44	£3,115.85	-£666.54	-£700.97	Removing high-risk subgroup reverts back to clinical parameters used in the original Rezum model [Settings!X21=No].
Basecase (all) - GreenLight (£540)	£2,404.64	£3,081.44	£3,115.85	-£676.78	-£711.22	Reducing cost of GreenLight to £540 to ensure consistent costs applied from the Rezum assessment report (MTG49, 2019) [EQUIPMENT!Q133=540]
Basecase (all): - GreenLight (£540) - HoLEP (remove amortalisation from capital costs)	£2,404.64	£3,081.44	£3,105.84	-£676.78	-£701.21	Reducing capital costs of HoLEP from £59.45 to £49.44 (when setting amortisation rate to 0% for the capital equipment), reduced the total costs by £10 as expected [EQUIPMENT!S189=0]
Basecase (all): - GreenLight (£540) - HoLEP (remove amortalisation from capital costs) - LoS for GreenLight and HoLEP 1.6 days - LoS for mTURP and bTURP 2.3 days	£2,739.21	£3,003.58	£2,967.14	-£264.36	-£227.93	NHS Reference costs 2019/20: - M65.3 Endoscopic resection of prostate NEC (TURP, which will combine mono- and bi-polar): *mean* length of stay 2.3 [Clinical - Procedure related resource use!N69 and P69=2.3] - M65.4 Endoscopic resection of prostate using laser (HoLEP and GreenLight combined): *mean* length of stay 1.6 [Clinical - Procedure related resource use!L69 and R69=1.6] Three Clinical experts stated that these estimates were reasonable.
Basecase (all): - GreenLight (£540) - HoLEP (remove amortalisation from capital costs)	£2,747.21	£3,062.97	£2,974.47	-£315.77	-£227.26	Including of erectile dysfunction outcomes after surgery has no impact on cost difference between GreenLight and HoLEP; this is due to the model assumption that erectile dysfunction outcomes would be the same for GreenLight and HoLEP.

Scenario	Mean discounted cost per patient (£), after 4 years (results from updated Company model			Cost difference (GreenLight-Comparator)		EAC Comment [Economic model setting changes]
	GreenLight	TURP	HoLEP	TURP	HoLEP	
- LoS for GreenLight and HoLEP 1.6 days - LoS for mTURP and bTURP 2.3 days - including erectile dysfunction outcomes						Inclusion of erectile dysfunction does increase cost saving associated with GreenLight when compared to TURP by an additional £51.41 over 4 years. However, the evidence used to apply this outcome to the economic model did not include GreenLight or HoLEP, and it should be considered that real cost savings over the whole BPH population might be appreciably less than this. The EAC would not consider this additional cost saving as robust. The EAC have derived these figures from the second table [Submission Tables B17-K29] and note that the intervention is listed as Rezum, not GreenLight. The EAC assume that the costs are reflective of GreenLight as the costs associated with device, theatre, hospital stay, pre- and post-tests, treating short-term adverse events, treating incontinence (repeat surgery) are the same as in the GreenLight arm where ED is not considered.
Basecase (all): - GreenLight (£540) - HoLEP (remove amortalisation from capital costs) - LoS for GreenLight and HoLEP 1 days - LoS for mTURP and bTURP 2 days	£2,512.34	£2,889.68	£2,748.14	-£377.33	-£235.80	NHS Reference costs 2019/20: - M65.3 Endoscopic resection of prostate NEC (TURP, which will combine mono- and bi-polar): *median* length of stay 2 [Clinical] - Procedure related resource use!N69 and P69=2] - M65.4 Endoscopic resection of prostate using laser (HoLEP and GreenLight combined): *median* length of stay 1 [Clinical - Procedure related resource use!L69 and R69=1]
Basecase (all): - GreenLight (£540) - HoLEP (remove amortalisation from capital costs)	£3,183.89	£3,649.03	£3,386.89	-£465.14	-£203.00	Data sourced from the GOLIATH study (Bachmann *et al.* 2014): - TURP: [Clinical - Procedure related resource use!N69 and P69=4]

Scenario	Mean discounted cost per patient (£), after 4 years (results from updated Company model			Cost difference (GreenLight-Comparator)		EAC Comment [Economic model setting changes]
	GreenLight	TURP	HoLEP	TURP	HoLEP	
- LoS for GreenLight and HoLEP 2.75 days - LoS for mTURP and bTURP 4 days						- GreenLight and HoLEP: [Clinical - Procedure related resource use!L69 and R69=2.75] Two Clinical Experts stated that the length of stay reported in GOLIATH trial are not representative and are much higher than current UK NHS practice.
Basecase (all): - GreenLight (£540) - HoLEP (remove amortalisation from capital costs) - LoS for GreenLight and HoLEP 1.6 days - LoS for mTURP and bTURP 2.3 days - 5% mono-polar	£2,739.63	£3,010.06	£2,967.14	-£270.43	-£227.51	Two Clinical experts advised that 25%/75% split between mono- and bi-polar TURP was a reasonable assumption. One Clinical expert stated that in their practice that more than 95% of TURP were bipolar [Settings!R35=5%].
Basecase (all): - GreenLight (£540) - HoLEP (remove amortalisation from capital costs) - LoS for GreenLight and HoLEP 1.6 days - LoS for mTURP and bTURP 2.3 days - 38% mono-polar	£2,738.95	£2,999.37	£2,967.14	-£260.42	-£228.20	One Clinical expert referenced the BAUS Bladder Outflow Obstruction audit, 2019 which included 332 cases of monopolar TURP and 548 cases of bipolar TURP (38% monopolar) [Settings!R35=38%].
Basecase (all): - GreenLight (£540) - HoLEP (remove amortalisation from capital costs) - LoS for GreenLight and HoLEP 1.6 days	£2,744.83	£3,003.58	£2,967.17	-£258.75	-£222.31	One Clinical expert advised that within their practice, that patients requiring surgical retreatment after GreenLight would undergo TURP surgery. Therefore the EAC modelled this scenario [Clinical – Treatment Effectiveness!L21=100] The EAC notes that another Clinical expert stated that some patients requiring surgical retreatment after TURP may

Scenario	Mean discounted cost per patient (£), after 4 years (results from updated Company model			Cost difference (GreenLight-Comparator)		EAC Comment [Economic model setting changes]
	GreenLight	TURP	HoLEP	TURP	HoLEP	
- LoS for mTURP and bTURP 2.3 days - 100% of surgical retreatments following GreenLight, conducted with TURP)						required HoLEP. However the Company economic model cannot be easily adapted to incorporate this scenario.
Basecase (all): - GreenLight (£540) - HoLEP (remove amortalisation from capital costs) - LoS for GreenLight and HoLEP 1.6 days - LoS for mTURP and bTURP 2.3 days - TURP procedure duration 49.6 min (same as GreenLight) - HoLEP procedure duration 60 mins	£2,733.96	£2,775.49	£2,697.20	-£41.53	+£36.76	One Clinical expert noted that HoLEP operating times could vary from 45 minutes to 3 hours, while another expert noted that HoLEP may be closer to 60 minutes in duration (EAC Correspondence Log, 2022). [Clinical – Procedure related resource use!N67 and P67=49.6] [Clinical – Procedure related resource use!R67=60] The EAC notes that the threshold procedure duration for HoLEP is 62.7 minutes, below this GreenLight is cost incurring, above this GreenLight is cost saving. Given the responses from Clinical experts, the EAC considers this plausible.
Basecase (all): - GreenLight (£540) - HoLEP (remove amortalisation from capital costs) - LoS for GreenLight and HoLEP 1.6 days - LoS for mTURP and bTURP 2.3 days -0.25% GreenLight surgeries converted to TURP	£2,741.22	3,003.58	2,967.14	-£262.36	-£225.92	Guided by device related adverse events from MAUDE database searches noting 0.1% of GreenLight cases requiring minor intervention or classed as moderate complication. The EAC assume that no surgeries would be converted to TURP as Trusts would not have access to both GreenLight and HoLEP lasers. The EAC have also not modelled scenario where TURP is converted to GreenLight as there is no evidence to suggest this is a plausible scenario. Two Clinical experts noted GreenLight conversion to TURP was a rare event occurring in around 1 in every 400 or 500 procedures (EAC Correspondence Log, 2022). This is in line with published evidence. Another expert reported this rate to

Scenario	Mean discounted cost per patient (£), after 4 years (results from updated Company model			Cost difference (GreenLight-Comparator)		EAC Comment [Economic model setting changes]
	GreenLight	TURP	HoLEP	TURP	HoLEP	
						be less than 10%, while another reported this to be much less than 1% (EAC Correspondence Log, 2022). The EAC have calculated the costs associated with intraoperative conversion to TURP as attributing the proportion of patients receiving clinical outcomes and parameters of TURP plus the device costs of GreenLight. [(0.9975*GreenLight)+ (0.0025*(TURP+£540))]
Basecase (all) - GreenLight (£500)	£2,363.68	£3,081.44	£3,115.85	-£717.76	-£752.17	Reducing the cost of GreenLight as suggested by the Company at fact-check. This increases potential costs savings of GreenLight when compared to TURP and HoLEP, as expected.
Basecase (all): - GreenLight (£500) - HoLEP (remove amortalisation from capital costs) - LoS for GreenLight and HoLEP 1.6 days - LoS for mTURP and bTURP 2.3 days - TURP procedure duration 49.6 min (same as GreenLight) - HoLEP procedure duration 60 mins	£2,693.00	£2,775.49	£2,697.20	-£82.49	-£4.20	Repeating scenario above which was cost-incurring compared to HoLEP, with the reduced cost of GreenLight (as recommended by the Company at fact-check) is now cost-saving compared to HoLEP.
Abbreviations: EAC, external assessment centre; LoS, length of stay; TURP, transurethral resection of the prostate; HoLEP, holmium laser enucleation of the prostate						

EAC base case

Given the limitations of the unpublished systematic review (Appendix B4) the EAC would not consider the clinical parameters nor the costs modelled for a high-risk population to be robust. The EAC considered modelling all patients as more appropriate, using the clinical parameters included within MTG49 (2019), which included GreenLight, TURP and HoLEP comparators, as the basis of its base case (Appendix E4). Additionally, the Company revised model (version 2) developed in Microsoft Excel was only partially executable, therefore the the EAC replicated the Company base case model (all patients) using R programming language (R Core Team, 2020) and the *rdecision* package (version 1.1.0). The EAC have applied a five-year time horizon to reflect the most robust comparative published literature available reporting retreatment rates to five years from the GOLIATH trial.

Clinical parameters

No additional randomised comparative evidence of GreenLight compared with HoLEP or TURP has been published since the original Assessment Report. Additionally, no additional randomised evidence was available for the different high-risk subgroups (prostate volume greater than 100 ml, patients with preoperative urine retention, or patients at high risk of bleeding).

The EAC noted the length of stay applied in the original decision tree economic model from 2016 used 10.36 days for HoLEP and GreenLight, and 10.65 days for TURP. Mean length of stay was updated for the assessment of Rezum (MTG49) to reflect lower mean lengths of stay across all technologies. As noted in Section 9.2, the EAC consider the length of stay of 1.6 days for GreenLight or HoLEP and 2.3 days for TURP to be more appropriate based on OPCS codes from NHS activity from 2019/20. Five Clinical experts agreed that these lower values of length of stay were more representative of current NHS practice (EAC Correspondence Log, 2022). The EAC did not include erectile dysfunction outcomes within the EAC base case due to lack of available data. The proportion of patients undergoing mono-polar TURP applied was 38% using latest data from the BAUS Bladder Outflow Obstruction audit, 2019. The EAC also included 0.25% of GreenLight patients requiring conversion to TURP due to surgical complications, which was identified

from the literature (Trujillo *et al.* 2021), MAUDE database search (Section 6), and confirmed by the Clinical experts (EAC Correspondence Log, 2022).

Cost parameters

To maintain a consistent source of cost parameters, the EAC reduced the cost of GreenLight to £540 in line with the value used in the Rezum Economic Submission (EAC Assessment Report, 2019). The EAC also removed discounting from the HoLEP capital equipment, and added the cost of saline bladder irrigation, in line with the approach taken in the decision tree model.

Results

Results from the EAC base case are presented in Table 26, showing GreenLight costing £2,787, TURP £3,092 and HoLEP £3,057 per procedure. This resulted in GreenLight being cost-saving of £305 compared with TURP, and cost-saving of £270 compared with HoLEP per patient over 5 years.

Table 26: EAC base case

Cost breakdown	Cost per patient (£), after 5 years (all patients)		
	GreenLight	TURP	HoLEP
Total Costs	**£2,787.14**	**£3,091.97**	**£3,056.66**
Net diff vs GreenLight	**-**	**-£304.83**	**-£269.52**

Sensitivity analysis

The EAC conducted a PSA around its base case (without ED adverse effects) using a restricted number of parameters considered to be uncertain. These were as follows:

- Proportion undergoing monopolar TURP (from BAUS Bladder Outflow Obstruction audit, 2019); 332 cases of monopolar TURP and 548 cases of bipolar TURP;
- Procedure duration for GreenLight, HoLEP, mono- and bi-TURP: Hyperparameters were based on Rezum Markov model by fitting to the confidence intervals using the method of moments. However, the confidence

intervals in Table 11 of the company submission for theatre time seem implausibly wide (e.g. HoLEP 40.1 mins to 120.3 mins) because the confidence intervals are supposed to represent uncertainty in the estimate of mean theatre time, *not* the centiles of the distribution of operating times themselves.

The mean cost difference from PSA between GreenLight and TURP was -£311.13 [95% CI -£894.41 to +£487.18] per patient, with 83.1% of simulations being cost-saving. The cost difference with HoLEP was -£265.30 [95% CI -£1171.35 to +£601.35] per patient, with 75.1% of simulations being cost-saving. However, the EAC would consider that the distributions applied to theatre time for each intervention arm are implausibly wide resulting in a large distribution in cost differences. The PSA is also limited by the number of parameters varied, which is a consequences of the lack of robust comparative or national audit data for key parameters such as procedure duration and length of stay for each intervention. Therefore, the EAC would consider that the results of PSA are not robust and may not be representative of cost savings in a UK NHS setting.

To account for the large uncertainty the EAC conducted additional univariate threshold analysis, and found that if the procedure duration of TURP and HoLEP reduced below 43.7 and 60.0 minutes respectively (relative to 49.6 minutes for GreenLight) then GreenLight would become cost-incurring. Similarly, if the length of hospital stay following TURP or HoLEP reduced below 1.5 and 0.9 days respectively (relative to 1.6 days for GreenLight) then GreenLight would become cost-incurring. However, as existing clinical coding is unable to distinguish GreenLight from HoLEP laser procedures (from where the 1.6 days length of stay was derived from) there remains uncertainty regarding length of stay across all arms. Additionally, Clinical experts have confirmed there is variation across centres in terms of day-case rates across BPH surgery (EAC Correspondence Log, 2022).

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

The EAC reviewed the decision tree economic model used by Birmingham and Brunel EAC to support the development of the original guidance for this topic, which had a six-month time horizon. Updating cost parameters only, the cost savings increased from £58.09 (corrected model) to £69.94 for GreenLight, when compared with TURP. However, the EAC found GreenLight to be slightly cost-incurring, by £114.43, when compared with HoLEP, when the previous base case had found it to be cost-saving by £851.13. This is due to the decreased capital costs for HoLEP associated with increased use each year, and this approach is in line with that used in MTG49. There remains a lack of comparative evidence regarding the proportion of day-case procedures across BPH interventions. However, the EAC used newly available UK evidence which reported 68% of GreenLight procedures were managed as day-case procedures (Trail *et al.* 2021), to perform univariate sensitivity analysis. This found GreenLight to be cost-saving by £373.01 when compared with TURP (assuming 4% day-case), and cost-saving by £188.63 when compared with HoLEP (assuming 36% day-case). If more than 43.6% of TURP procedures or more than 56% of HoLEP procedures were conducted as day-case procedures, then GreenLight becomes cost-incurring if the proportion of GreenLight procedures conducted as a day-case remains fixed at 68%.

The Company submitted an updated economic model based on the Markov model originally developed for Rezum (MTG49, also manufactured by Boston Scientific), which included GreenLight, TURP and HoLEP arms, in line with the decision problem of this GreenLight assessment report update. The Company applied data from an unpublished systematic review to model a high-risk population. The unpublished systematic review was poorly reported, lacked transparency, and the outcomes lacked clinical validity. The EAC only identified two studies comparing GreenLight with TURP exclusively conducted in high-risk populations reporting on length of stay and readmission outcomes only; both studies were conducted in France with small sample sizes and included some patients with other high-risk factors not listed in the Scope. Therefore, the EAC disregarded the exclusive modelling of high-risk patients due to lack of robust evidence. The EAC reverted to using the clinical parameters applied in the original Rezum model, and conducted scenario analysis to generate an economic model that was more generalisable to a

BPH population, including patients considered high-risk. The EAC base case (which decreased the cost of GreenLight, removed amortalisation from capital HoLEP costs, decreased the length of stay across all arms as informed by Clinical experts, and increased the proportion of mono-TURP in line with national audit data) found GreenLight to be cost saving by approximately £305 and £270 per patient over 5 years when compared with TURP and HoLEP respectively. PSA was limited by lack of data on key parameters such as length of stay and procedural duration, but still found GreenLight to be cost-saving in 83% of simulations when compared with TURP, and in 75% when compared with HoLEP. Univariate threshold analysis conducted by the EAC found that if the procedure duration and length of stay of TURP was similar to GreenLight, or if the HoLEP procedural duration was one hour or less, then GreenLight would become cost-incurring. Both of these are clinically plausible. The EAC notes that extended procedure duration and extended length of stay may be required in some high-risk patients (for example, patients with large prostates).

The EAC would conclude that both economic models (original decision tree and updated Markov model) demonstrate the potential for GreenLight to be cost-saving when compared with TURP and HoLEP. However, due to the lack of comparative evidence there remains some uncertainty regarding the magnitude of cost savings.

10 Conclusions

10.1 *Conclusions from the clinical evidence*

There is agreement from the Clinical experts that GreenLight 180 W XPS PVP is used routinely in the NHS. No additional randomised evidence has been published since the original assessment report. GreenLight PVP is associated with a shorter post-operative catheterisation period (Reimann *et al.* 2019; Cimino *et al.* 2017; Mattevi *et al.* 2017), shorter hospital stay (Gondran-Tellier *et al.* 2021; Reimann *et al.* 2019; Mathieu *et al.* 2017; Mattevi *et al.* 2017), and higher ejaculatory function at 12 months (Cimino *et al.* 2017) when compared with TURP. There is consensus among Clinical experts and the literature that GreenLight XPS 180 W PVP can be undertaken as a day-case procedure within an NHS setting (EAC Correspondence Log; Trail *et al.* 2019). Eight of eleven clinical experts suggest GreenLight XPS procedure would be particularly beneficial in patients considered at high risk, elderly or on anticoagulation therapy (EAC Correspondence Log, 2022).

The majority of studies (50 of 58) included patients considered of high-risk, only 2 comparative studies (Gondran-Tellier *et al.* 2021; Mesnard *et al.* 2021) and 2 retrospective cohorts (Meskawi *et al.* 2017; Eken and Soyupak 2018) were conducted exclusively in high-risk patients. Eight identified cohort studies, which subgrouped patients by risk factor, were retrospective, included patients with comorbidities and as such potentially confounded the effect due to GreenLight alone. The EAC notes that studies included patients with multiple risk factors.

One retrospective cohort study (Campobasso *et al.* 2020) subgrouped patients by prostate size (n=1,031 patients, 916 with prostate volume less than 100 ml, 115 greater or equal to 100 ml); however 16.3% had history of indwelling catheter (with a significant difference in the proportion of patients with indwelling catheter between subgroups), 30.5% were taking antiplatelet and 8.8% taking anticoagulation (but with no significant difference in the proportion of patients taking antiplatelet or anticoagulant medication found between subgroups). This study reported no significant difference in IPSS, Qmax, length of post-operative stay, duration of catheterisation between prostate size subgroups. A significant difference in early complications, and later complications was reported between subgroups, and the

duration of follow-up was significantly different (longer) in the large prostate subgroup.

Four retrospective cohort studies subgrouped by anticoagulation status. Lee *et al.* (2016) (186 patients taking anticoagulant or antiplatelet medication, and 198 patients taking neither, with no difference in prostate volume or proportion in preoperative retention between subgroups) reported a significant difference in conversion to TURP and length of stay between subgroups. However, no difference was reported in intraoperative bleeding, duration in catheterisation, IPSS, Qmax, PVR or QoL between subgroups at 24 months. Knapp *et al.* (2017) (59 patients taking anticoagulation, 42 aspirin, 272 taking neither) reported a significant difference in duration of catheterisation and length of stay between patients taking anticoagulation and those not, but no difference between patients taking aspirin and those not. No difference in overall adverse events was reported between subgroups, with no blood transfusions required, however more high-grade complications were reported in the anticoagulation arm. Meskawi *et al.* (2019) (37 patients taking anticoagulation, 87 aspirin, 24 other antiplatelets, 274 taking none; with a significant difference in prostate volume between subgroups) reported a significant difference in need for transfusion (occurring in aspirin and antiplatelet arms only), length of catheterisation, duration of hospital stay and readmission within 30 days between subgroups. No difference in retreatment rates or requirement of long-term intermittent or permanent catheterisation was found between subgroups. Eken and Soyupak (2018) (59 patients taking antiplatelet or anticoagulant, and 174 taking none; age and ASA score significantly different between groups) reported no significant difference in dysuria or bleeding between subgroups. The study reported that no transfusions were required in any patient.

One retrospective cohort study (Goueli *et al.* 2017) subgrouped patients by preoperative urine retention status (n=332 patients, 137 with preoperative urine retention and 195 without, with significant difference in prostate volume between subgroups; 37% taking anticoagulation with no significant difference between subgroups). The study reported no significant difference in IPSS, Qmax, PVR and QoL between the urinary retention subgroups (Goueli *et al.* 2017). A significant difference in duration of catheterisation, length of hospital stay and proportion of

patients experiencing complications within 90 days were reported between the subgroups.

There is a large amount of evidence on safety and efficacy, and in clinical guidelines (EUA, CUA, AUA) supporting the continued use of GreenLight XPS 180 W PVP for treating patients with BPH within the NHS. Whilst occurrence of adverse events are low even in high-risk groups, availability of blood (in patients requiring a transfusion) and beds (in patients requiring increased observation) are advised.

10.2 *Conclusions from the economic evidence*

No additional randomised comparative evidence for GreenLight compared with HoLEP or TURP has been published since the original Assessment Report. There is not enough robust evidence to model high-risk patients exclusively. Six published economic studies were identified, none were conducted in the UK and therefore lacked generalisability to the NHS. Four of the six identified economic studies reported GreenLight to be cost-effective or cost-saving compared with TURP (Caicedo *et al.* 2019, Masucci *et al.* 2018, Erman *et al.* 2018, Ulchaker and Martinson 2018). Brown *et al.* (2019) reported no significant difference in costs between TURP and GreenLight PVP, and Mathieu *et al.* (2017) reported GreenLight to be significantly more expensive than TURP and HoLEP in prostates smaller than 80 ml. In general, the factors identified in the evidence as having an impact on costs were comorbidities, length of stay, readmissions and device costs.

By updating only the cost parameters only of the original short-term decision tree model, GreenLight was found to be cost-saving by £69.94 when compared with TURP, and cost-incurring by £114.43 when compared with HoLEP at 6 months. Cost savings increased if the proportion of GreenLight procedures conducted as a day-case increased, however, there was uncertainty regarding the proportion of TURP and HoLEP procedures performed as day-cases. When utilising a longer-term Markov model, the point estimates of cost-saving with GreenLight were £305 and £270 when compared with TURP and HoLEP respectively at 5 years. PSA conducted by the EAC showed GreenLight to be cost saving in 83% and 75% of simulations when compared with TURP and HoLEP respectively. However, there remains uncertainty regarding length of stay and procedural duration across intervention and comparator arms, which could not be addressed in PSA due to lack

of data. Threshold analysis (of the comparator arms) found GreenLight to be cost-incurring at clinically plausible values of length of stay and procedural duration for TURP and HoLEP.

11 Summary of the combined clinical and economic sections

A total of 58 publications relevant to the decision problem were identified; the EAC focused on the 37 most relevant (11 comparative, 8 exclusively in high-risk population or subgroup, 1 cohort reporting on day-case procedures, 17 single-arm studies reporting on rare adverse outcomes or day-case procedures). No additional randomised evidence comparing GreenLight against TURP was identified. There remains no randomised evidence comparing GreenLight to HoLEP. The clinical evidence included was of low to good quality, with only one conducted in a UK NHS setting. The evidence continues to support the use of GreenLight 180 W XPS as an available option in patients with BPH for symptomatic relief, with clinical benefits also realised in high-risk patient groups (prostate volume greater than 100 ml, patients with preoperative urine retentions, patients at risk of bleeding) with low occurrence of adverse events.

Six published economic studies were identified, two of which demonstrated GreenLight to be cost-saving when compared with TURP, one showed GreenLight to be more costly but more cost effective than TURP, and one cost-saving when compared to HoLEP/ThuLEP (interventions were not reported exclusively). The results of two economic evaluations (short-term decision tree or long-term Markov model) consistently report the potential for cost savings associated with GreenLight when compared with TURP and HoLEP. Some scenarios (increased day-case, reduced length of stay, reduced procedural duration of the comparator arms) result in GreenLight to be cost-incurring. However, due to lack of robust data, and variation in both clinical practice and variation in patient risk profile, there remains some uncertainty regarding the magnitude of cost-savings.

12 Implications for research

The GOLIATH trial, which was considered within the original assessment report, remains the only randomised evidence comparing GreenLight against TURP (mono- and bi-polar combined). No randomised evidence comparing GreenLight 180 W PVP with HoLEP has been identified. The majority of evidence published since NICE guidance on GreenLight (MTG29, 2016) has included high-risk patients; only one UK study (Trail *et al.* 2021) was identified that included patients with pre-operative urine retention but not exclusively. Due to the increased risk of bleeding, complications and longer hospital stays associated with TURP, further randomised studies, comparing with GreenLight in a UK NHS setting exclusively in high-risk patients, is likely to be considered unethical.

There are remaining uncertainties in the procedure duration and length of stay associated with GreenLight, TURP and HoLEP in an NHS setting, which are important to the economic case. There is also a lack of longitudinal evidence that maps out the pathway of patients requiring one or more BPH interventions. Currently available clinical coding (OPCS procedure codes) are unable to distinguish the types of BPH surgery, and also do not capture prostate volume or severity of lower urinary tract symptoms (ICD10 diagnosis codes), therefore it is not possible to conduct retrospective analysis of routine data from Hospital Episode Statistics to robustly compare GreenLight with TURP and HoLEP. However, service evaluation or multi-centre audit studies would help address this evidence gap.

Comparison of enucleation techniques as alternative treatments of BPH (for example GreenLEP compared with HoLEP) are out of scope of this assessment report update, and would require a separate assessment.

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14 Appendices

Appendix A: Clinical literature search

Appendix A1a: PRESS checklist completed by the NICE EAC for the Company literature search 2021

Question	Y/N	Notes
Does the search strategy match the research question/PICO?	Yes	The search strategy has two main components: prostate hypertrophy AND Greenlight
Are the search concepts clear?	No	Line 1 to 3 has some redundant concepts
Are there too many or too few PICO elements included?	Okay	Condition AND Intervention
Are the search concepts too narrow or too broad?	Both	Boston, lasers, laser, are broad
Does the search retrieve too many or too few records? (Please show number of hits per line.)		Difficult to ascertain
Are unconventional or complex strategies explained?	No	No explanation is given
Are Boolean or proximity operators used correctly?	Yes	The search uses Boolean operators correctly to combine the two main concepts. The search uses adjacency within concepts
Is the use of nesting with brackets appropriate and effective for the search?	Yes	
If NOT is used, is this likely to result in any unintended exclusions?	Possibly	NOT is used to exclude conference abstracts but unsure of how that exclusion performs.
Could precision be improved by using proximity operators (*e.g.*, adjacent, near, within) or phrase searching instead of AND?	Yes	Distant proximity is used in line 2. The set retrieves many results, although sensitivity is maximised by using a distant proximity operator, precision is not. Further, this set almost supersedes line 1, and seems redundant.
Is the width of proximity operators suitable (*e.g.*, might adj5 pick up more variants than adj2)?	Probably not	Difficult to ascertain. Line 6 seems to use unnecessary distant (6 words away) adjacency for a concept that is possibly not more than 3 words away as standard.

		The set retrieves a large amount of results. Line 5 and Line 6 seem to overlap and could have been rationalised.
Are the subject headings relevant?	No	The Company ran their search on Embase.com and so there may be functionality available via that platform that is not available using Ovid. The Company appeared to use Emtree term that are not available on the Ovid platform. As far as Embase (on Ovid) Emtree thesaurus is concerned there is no greenlight laser/ or greenlight/ or photoselective vaporization of the prostate/ or photoselective vaporisation/ I cannot explain how line 3 retrieves 143 results, since none of the search terms entered on that line actually map to any Emtree term in Ovid.
Are any relevant subject headings missing; for example, previous index terms?	Yes	Relevant Emtree terms that could have been used would be laser surgery/ a very broad term, or laser prostatectomy/ a narrower term
Are any subject headings too broad or too narrow?	N/A	Due to the possible differences in Emtree terms available between the Embase.com and Ovid platforms it is not possible to judge where subject headings were appropriate or existent.
Are subject headings exploded where necessary and vice versa?	Yes	The use of explosion for thesaurus terms is not appropriate. For instance, Prostate hypertrophy/ can't be exploded as there are no narrower terms under this thesaurus entry.
Are major headings ("starring" or restrict to focus) used? If so, is there adequate justification?	N/A	
Are subheadings missing?	N/A	
Are subheadings attached to subject headings? (Floating subheadings may be preferred.)	No	
Are floating subheadings relevant and used appropriately?	N/A	

Are both subject headings and terms in free text (see the following) used for each concept?	No	
Does the search include all spelling variants in free text (*e.g.*, UK vs. US spelling)?	No	The search missed vapourisation OR vapourization; the use of hyphenated terms such as green-light OR photo-selective
Does the search include all synonyms or antonyms (*e.g.*, opposites)?	No	Hyphenated terms are missing such as 180-w; 120-w; 80-w
Does the search capture relevant truncation (i.e., is truncation at the correct place)?	No	Greenlight* will pick up GreenlightTM or GreenlightXPS Moxy* will pick up MoxyTM
Is the truncation too broad or too narrow?	No	When used, truncation appears adequate, with such that, not too broad or too narrow.
Are acronyms or abbreviations used appropriately? Do they capture irrelevant material? Are the full terms also included?	No	Many acronyms used and not included in their full extended version such as ktp, bph, bpe, lbo
Are the keywords specific enough or too broad? Are too many or too few keywords used? Are stop words used?	Yes	Some redundancy in the use of keywords has been detected, with such that, between line 6 and line 5 of the MEDLINE search strategy
Have the appropriate fields been searched; for example, is the choice of the text word fields (.tw.) or all fields (.af.) appropriate? Are there any other fields to be included or excluded (database specific)?	Uncertain	The Embase search via Embase.com does not specify fields. Since I am not familiar with the interface and don't have access to it I can't ascertain whether the lack of specific fields in the search is due to the platform or neglect of the search strategy designer
Should any long strings be broken into several shorter search statements?	Yes	Long strings should be rationalised and redundancy removed
Are there any spelling errors?	No	
Are there any errors in system syntax; for example, the use of a truncation symbol from a different search interface?	No	The asterisk is used for truncation throughout the Embase search via Embase.com. This symbol is supported in Embase Ovid, I have no reason to suspect it not being supported in Embase.com. Can't test it though.
Are there incorrect line combinations or orphan lines (i.e., lines that are not referred to in the final summation that	Yes	Line 9 is superfluous.

could indicate an error in an AND or OR statement)?		
Are all limits and filters used appropriately and are they relevant given the research question?	Possibly not	Time limits could have been used more efficiently. No reasons are given for the removal of conference abstracts. The scope specifies searching for “clinical studies” but then it also includes meta-analyses and systematic reviews. Conference abstracts are removed by using the indexing term, all those conference abstracts not indexed yet, would have been kept.
Are all limits and filters used appropriately and are they relevant for the database?	Possibly not	See above
Are any potentially helpful limits or filters missing? Are the limits or filters too broad or too narrow? Can any limits or filters be added or taken away?	N/A	
Are sources cited for the filters used?	N/A	

Appendix A1b: PRESS checklist for original Birmingham NICE EAC literature search conducted in 2015 for the original guideline

Question	Y/N	Notes
Translation of the research question		
Does the search strategy match the research question/PICO?	Yes	Only terms condition AND intervention included
Are the search concepts clear?	Yes	
Are there too many or too few PICO elements included?	Okay	Given these searches are not designed for a systematic literature review the selection of PICO elements included in the original search strategy seems reasonable.
Are the search concepts too narrow or too broad?	Yes	Combination of broad concepts such as Laser Therapy/ with very narrow ones such as 180-w xps (line 10 in MEDLINE search strategy). No additional lines to break down this concept were made in the search
Does the search retrieve too many or too few records? (Please show number of hits per line.)	N/A	Difficult to ascertain, what is too many in the context of this topic? Other more focussed searches would have retrieved less records.
Are unconventional or complex strategies explained?	No	Not clear why concepts were combined in that manner in the original searches: (BPH AND Laser Therapy/) OR (BPH AND greenlight-related terms) Almost feels as if they were trying to compare the size of the literature in those two topics. Further, the MEDLINE therapy "maximizes sensitivity" filter was applied to both concepts and it is unsure the impact this might have had on the ability to retrieve relevant records
Boolean and proximity operators (these vary based on search service)		
Are Boolean or proximity operators used correctly?	Yes	The use of Boolean operators per line and per concept is appropriate.
Is the use of nesting with brackets appropriate and effective for the search?	N/A	This feature is not used
If NOT is used, is this likely to result in any unintended exclusions?	N/A	
Could precision be improved by using proximity operators (*e.g.*, adjacent, near, within) or	Yes	

phrase searching instead of AND?		
Is the width of proximity operators suitable (*e.g.*, might adj5 pick up more variants than adj2)?	N/A	
Subject headings (database specific)		
Are the subject headings relevant?	Yes	One subject heading was not translated into a free text search, with such that, Laser Therapy/ (although as noted below this term may have been too broad)
Are any relevant subject headings missing; for example, previous index terms?	No	
Are any subject headings too broad or too narrow?	Yes	Laser Therapy/ is too broad Laser coagulation/ could have been used instead
Are subject headings exploded where necessary and vice versa?	No	The only heading that could have been exploded was Laser Therapy/ which would have included the relevant Laser Coagulation/ subject heading, as this heading wasn't exploded all indexed papers under Laser Coagulation/ would not have been retrieved by this search
Are major headings ("starring" or restrict to focus) used? If so, is there adequate justification?	N/A	
Are subheadings missing?	No	
Are subheadings attached to subject headings? (Floating subheadings may be preferred.)	No	
Are floating subheadings relevant and used appropriately?	N/A	
Are both subject headings and terms in free text (see the following) used for each concept?	Okay	Mostly, Laser Therapy/ has not a free text equivalent search line (although as mentioned above this may have been too broad a term to use).
Text word searching (free text)		
Does the search include all spelling variants in free text (*e.g.*, UK vs. US spelling)?	No	Vaporisation/vaporization could be spelt as vapourisation or vapourization GreenLight could be spelt as two words green light with hyphen or without. These variations have not been considered in the original search

Does the search include all synonyms or antonyms (*e.g.*, opposites)?	No	Prostatic hyperplasia could be described using more terms such as prostatic hypertrophy
Does the search capture relevant truncation (i.e., is truncation at the correct place)?	No	Prostat* could capture prostatic or prostate; Hyperplas* could capture hyperplasia or hyperplastic Enlarg* could capture enlarged or enlargement
Is the truncation too broad or too narrow?	N/A	No truncation has been used
Are acronyms or abbreviations used appropriately? Do they capture irrelevant material? Are the full terms also included?	No	BPH is missing; Line 7 for PVP (abbreviation for "photoselective vapori#ation" is searched alone and captures noise)
Are the keywords specific enough or too broad? Are too many or too few keywords used? Are stop words used?	Y/N	The key words used are specific but the way in which they have been used makes the search retrieve noise, with such that, lines 5 or 7 (too broad) or line 10 (too specific). More keywords could have been used to increase sensitivity. This search is missing the manufacturer's key word related terms.
Have the appropriate fields been searched; for example, is the choice of the text word fields (.tw.) or all fields (.af.) appropriate? Are there any other fields to be included or excluded (database specific)?	No	The search uses mp. in MEDLINE Ovid this field searches a range of fields such as mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier Some of the fields searched by mp. are not relevant to the search concepts in this case.
Should any long strings be broken into several shorter search statements?	N/A	No long strings
Spelling, syntax, and line numbers		
Are there any spelling errors?	No	Negative if we consider the lack of alternative spellings (with such that, British/American, hyphen/not hyphen) not a spelling mistake but a search mistake
Are there any errors in system syntax; for example, the use of a truncation symbol from a different search interface?	No	

Are there incorrect line combinations or orphan lines (i.e., lines that are not referred to in the final summation that could indicate an error in an AND or OR statement)?	No	
Limits and filters		
Are all limits and filters used appropriately and are they relevant given the research question?	Y/N	There are limits used for “therapy (maximizes sensitivity)” this is a ready-made filter available in Ovid. I am not certain of its performance or how it is built. When applying a filter, it would be better if the search strategy is visible so can be appraised. Limiting to therapy in this case is relevant to the search question.
Are all limits and filters used appropriately and are they relevant for the database?	Yes	The filter used is an Ovid filter, applicable to MEDLINE and Embase.
Are any potentially helpful limits or filters missing? Are the limits or filters too broad or too narrow? Can any limits or filters be added or taken away?	Yes	A filter to exclude animal studies could have been used
Are sources cited for the filters used?	No	
Further comments:		
This PRESS checklist has been applied to the Medline and EMBASE OVID search strategies undertaken by the Birmingham NICE EAC: originally searched on 5/6th October 2015 and subsequently re-run on 13 of November 2015.		

Appendix A2: Literature search conducted by NICE EAC in November 2021 for the guideline update (GID-MT564 GreenLight XPS for BPH)

Database and years covered by the search (where applicable)	Dates of coverage	Date of search	Number of records
Ovid MEDLINE(R) 1946 to November Week 3 2021	1946 to November Week 5 2021	15/12/2021	283
Ovid MEDLINE(R) In-Process & In-Data-Review Citations	1946 to November 24, 2021	25/11/2021	24
Ovid MEDLINE(R) Daily Update November 24, 2021	November 24, 2021	25/11/2021	1
Ovid MEDLINE(R) Epub Ahead of Print November 24, 2021	November 24, 2021	25/11/2021	15
Embase (via Ovid)	1974 to 2021 November 24	25/11/2021	367
HTA (via CRD Database website)	For HTA up to 31 March 2018, when active updating of these databases ended. Content has now been transferred to INAHTA and new records are added regularly – only INAHTA was searched for this guideline update.	Not applicable – see dates of coverage here and INAHTA below	N/A
Cochrane Library (via Wiley) - Cochrane Database of Systematic Reviews	From inception to November 2021	29/11/2021	1
Cochrane Library (via Wiley) - CENTRAL	From inception to November 2021	29/11/2021	149
INAHTA	From inception to November 2021	30/11/2021	4
IDEAS/RePEC	From inception to November 2021	30/11/2021	5
WHO ICTRP	From inception to November 2021	30/11/2021	66
ClinicalTrials.gov	From inception to November 2021	30/11/2021	35
Total number of records retrieved from all sources			950
Total number of records after de-duplication			544

Three separate searches were performed in Ovid MEDLINE as described below. Together they retrieved a greater number of records (total n=283 potential duplicates not removed) than searching directly Ovid MEDLINE® and Epub Ahead of Print, In-Process & In-Data-Review Citations, Daily and Versions® (n= 265)

Source: Ovid MEDLINE(R) 1946 to November Week 3 2021

Interface/URL: OvidSP
Database coverage dates: 1946 to present
Search date: 25/11/2021
Retrieved records: 258
Ovid MEDLINE(R) <1946 to November Week 3 2021>

1 Prostatic Hyperplasia/ 22830

2 prostat* hyperplas*.ti,ab,kf. 15013

3 prostat* obstruction.ti,ab,kf. 850

4 (prostat* adj3 (hypertroph* or enlarg*)).ti,ab,kf. 5539

5 prostat* adenoma*.ti,ab,kf. 1112

6 (BPH or BPO or BPE).ti,ab,kf. 12500

7 or/1-6 31044

8 (greenlight or greenlight* or XPS-greenlight or greenlight-XPS* or "greenlight XPS*" or "green light" or green-light).ti,ab,kf. 2572

9 (Moxy or Moxy*).ti,ab,kf. 42

10 or/8-9 2604

11 photo-selective vapo?ri#ation.ti,ab,kf. 13

12 photoselective vapo?ri#ation.ti,ab,kf. 393

13 ((vapo?ri* adj3 prostat*) or (laser adj3 vapo?ri*) or (pvp adj6 (prostat* or laser))).ti,ab,kf. 1578

14 or/11-13 1594

15 "boston scientific".ix,ia,ir,go,ci. 1779

16 10 or 14 or 15 5677

17 7 and 16 787

18 limit 17 to english language 654

19 animals/ not humans/ 4883389

20 18 not 19 641

21 (20151$ or 2016$ or 2017$ or 2018$ or 2019$ or 2020$ or 2021$).ed. 5881734

22 20 and 21 258

Source: Ovid MEDLINE(R) In-Process & In-Data-Review Citations <1946 to November 24, 2021>

Interface/URL: Ovid MEDLINE(R) In-Process & In-Data-Review Citations <1946 to November 24, 2021>

Database coverage dates: 1946 to present
Search date: 25/11/2021
Retrieved records: 24

Ovid MEDLINE(R) In-Process & In-Data-Review Citations <1946 to November 24, 2021>

1 Prostatic Hyperplasia/0

2 prostat* hyperplas*.ti,ab,kf. 231

3 prostat* obstruction.ti,ab,kf. 25

4 (prostat* adj3 (hypertroph* or enlarg*)).ti,ab,kf. 48

5 prostat* adenoma*.ti,ab,kf. 2

6 (BPH or BPO or BPE).ti,ab,kf. 199

7 or/1-6 317

8 (greenlight or greenlight* or XPS-greenlight or greenlight-XPS* or "greenlight XPS*" or "green light" or green-light).ti,ab,kf. 61

9 (Moxy or Moxy*).ti,ab,kf. 1

10 or/8-9 62

11 photo-selective vapo?ri#ation.ti,ab,kf. 4

12 photoselective vapo?ri#ation.ti,ab,kf. 15

13 ((vapo?ri* adj3 prostat*) or (laser adj3 vapo?ri*) or (pvp adj6 (prostat* or laser))).ti,ab,kf. 25

14 or/11-13 25

15 "boston scientific".ix,ia,ir,go,ci. 214

16 10 or 14 or 15 287

17 7 and 16 25

18 limit 17 to english language 24

19 animals/ not humans/ 0

20 18 not 19 24

Source: Ovid MEDLINE(R) Daily Update November 24, 2021

Interface/URL: Ovid MEDLINE(R) Daily Update November 24, 2021

Database coverage dates: 1946 to present
Search date: 25/11/2021
Retrieved records: 1

Ovid MEDLINE(R) Daily Update <November 24, 2021>

1 Prostatic Hyperplasia/ 10

2 prostat* hyperplas*.ti,ab,kf. 11

3 prostat* obstruction.ti,ab,kf. 0

4 (prostat* adj3 (hypertroph* or enlarg*)).ti,ab,kf. 3

5 prostat* adenoma*.ti,ab,kf. 0

6 (BPH or BPO or BPE).ti,ab,kf. 11

7 or/1-6 15

8 (greenlight or greenlight* or XPS-greenlight or greenlight-XPS* or "greenlight XPS*" or "green light" or green-light).ti,ab,kf. 3

9 (Moxy or Moxy*).ti,ab,kf. 0

10 or/8-9 3

11 photo-selective vapo?ri#ation.ti,ab,kf. 0

12 photoselective vapo?ri#ation.ti,ab,kf. 0

13 ((vapo?ri* adj3 prostat*) or (laser adj3 vapo?ri*) or (pvp adj6 (prostat* or laser))).ti,ab,kf. 0

14 or/11-13 0

15 "boston scientific".ix,ia,ir,go,ci. 16

16 10 or 14 or 15 19

17 7 and 16 1

18 limit 17 to english language 1

19 animals/ not humans/ 2089

20 18 not 19 1

Source: Ovid MEDLINE(R) Epub Ahead of Print November 24, 2021

Interface/URL: Ovid MEDLINE(R) Epub Ahead of Print November 24, 2021

Database coverage dates: 1946 to present
Search date: 25/11/2021
Retrieved records: 15

Ovid MEDLINE(R) Epub Ahead of Print <November 24, 2021>

1 Prostatic Hyperplasia/0

2 prostat* hyperplas*.ti,ab,kf. 229

3 prostat* obstruction.ti,ab,kf. 18

4 (prostat* adj3 (hypertroph* or enlarg*)).ti,ab,kf. 59

5 prostat* adenoma*.ti,ab,kf. 3

6 (BPH or BPO or BPE).ti,ab,kf. 209

7 or/1-6 326

8 (greenlight or greenlight* or XPS-greenlight or greenlight-XPS* or "greenlight XPS*" or "green light" or green-light).ti,ab,kf. 58

9 (Moxy or Moxy*).ti,ab,kf. 0

10 or/8-9 58

11 photo-selective vapo?ri#ation.ti,ab,kf. 0

12 photoselective vapo?ri#ation.ti,ab,kf. 10

13 ((vapo?ri* adj3 prostat*) or (laser adj3 vapo?ri*) or (pvp adj6 (prostat* or laser))).ti,ab,kf. 29

14 or/11-13 29

15 "boston scientific".ix,ia,ir,go,ci. 283

16 10 or 14 or 15 363

17 7 and 16 15

18 limit 17 to english language 15

19 animals/ not humans/ 0

20 18 not 19 15

Source: Ovid Embase 1974 to 2021 December 15

Interface/URL: OvidSP
Database coverage dates: 1974 to present
Search date: 16/12/2021
Retrieved records: 367

Embase <1974 to 2021 December 15>

1 prostate hypertrophy/ 38655

2 prostat* hyperplas*.ti,ab,kw. 24363

3 prostat* obstruction.ti,ab,kw. 1394

4 (prostat* adj3 (hypertroph* or enlarg*)).ti,ab,kw. 7266

5 prostat* adenoma*.ti,ab,kw. 1358

6 (BPH or BPO or BPE).ti,ab,kw. 22232

7 or/1-6 50358

8 (greenlight or greenlight* or XPS-greenlight or greenlight-XPS* or "greenlight XPS*" or "green light" or green-light).ti,ab,kw. 4470

9 (Moxy or Moxy*).ti,ab,kw. 102

10 or/8-9 4528

11 photo-selective vapo?ri#ation.ti,ab,kw. 68

12 photoselective vapo?ri#ation.ti,ab,kw. 853

13 ((vapo?ri* adj3 prostat*) or (laser adj3 vapo?ri*) or (pvp adj6 (prostat* or laser))).ti,ab,kw. 3049

14 or/11-13 3076

15 "boston scientific".ae,au,dm,dv,in,pc,go. 24213

16 10 or 14 or 15 30996

17 7 and 16 1761

18 limit 17 to english language 1598

19 (animal/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not exp human/ 6349079

20 (conference abstract or conference paper or conference proceeding or conference review).pt. 5048035

21 19 or 20 11029451

22 18 not 21 835

23 (201510$ or 2016$ or 2017$ or 2018$ or 2019$ or 2020$ or 2021$).yr,dp,dc. 10621034

24 22 and 23 370

25 remove duplicates from 24 367

Source: Cochrane Database of Systematic Reviews (CDSR) and Cochrane Central Register of Controlled Trials (CENTRAL) - Issue 11 of 12, November 2021

Interface/URL: Cochrane Library, Wiley
Database coverage dates: 1995 to present
Search date: 29/11/2021
Retrieved records: 150
CDSR: 1
CENTRAL: 149

ID Search Hits

#1 MeSH descriptor: [Prostatic Hyperplasia] this term only 1833

#2 (prostat* NEXT hyperplas*):ti,ab,kw 3462

#3 (prostat* NEXT obstruction):ti,ab,kw 210

#4 (prostat* NEAR/3 hypertroph*):ti,ab,kw 1822

#5 (prostat* NEAR/3 enlarg*):ti,ab,kw 420

#6 (prostat* NEXT adenoma*):ti,ab,kw 96

#7 ((BPH or BPO or BPE)):ti,ab,kw 2544

#8 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 4585

#9 (greenlight or greenlight* or XPS-greenlight or greenlight-XPS* or (greenlight NEXT XPS*) or "green light" or green-light):ti,ab,kw 286

#10 (Moxy or Moxy*):ti,ab,kw 14

#11 #9 OR #10 293

#12 (photo-selective vapo?ri*ation):ti,ab,kw 9

#13 (photoselective vapo?ri*ation):ti,ab,kw 120

#14 (vapo?ri* NEAR/3 prostat*):ti,ab,kw 203

#15 (laser NEAR/3 vapo?ri*):ti,ab,kw 182

#16 (pvp NEAR/6 (prostat* OR laser)):ti,ab,kw 109

#17 #12 OR #13 OR #14 OR #15 OR #16 333

#18 "boston scientific":au,so,ab,kw,ti 576

#19 #11 OR #17 OR #18 1095

#20 #8 AND #19 with Cochrane Library publication date Between Oct 2015 and Nov 2021 150

Source: International HTA Database

Interface/URL: https://database.inahta.org/search/advanced
Database coverage dates: since inception
Search date: 30/11/2021
Retrieved records: 4

Search query, Hits, time limits 2015 to 2021

(((boston scientific)) OR ((((vapo* AND prostat*)) OR ((laser AND vapo*)) OR ((pvp AND prostat*)) OR ((pvp AND laser))) OR ((photo-selective vapo*) OR (photoselective vapo*))) OR (((Moxy or Moxy*)) OR ((greenlight OR greenlight* OR XPS-greenlight OR greenlight-XPS* OR greenlight XPS* OR green light OR green-light)))) AND (((prostatic hyperplasia)[mh])[mh] OR (prostatic hyperplas*) OR (prostat* hyperplasia) OR (prostat* obstruction) OR ((prostat* adenoma) OR (prostat* adenomas)) OR ((BHP OR BPO OR BPE))), 28

((boston scientific)) OR ((((vapo* AND prostat*)) OR ((laser AND vapo*)) OR ((pvp AND prostat*)) OR ((pvp AND laser))) OR ((photo-selective vapo*) OR (photoselective vapo*))) OR (((Moxy or Moxy*)) OR ((greenlight OR greenlight* OR XPS-greenlight OR greenlight-XPS* OR greenlight XPS* OR green light OR green-light))), 393

(boston scientific), 11

(((vapo* AND prostat*)) OR ((laser AND vapo*)) OR ((pvp AND prostat*)) OR ((pvp AND laser))) OR ((photo-selective vapo*) OR (photoselective vapo*)), 35

((vapo* AND prostat*)) OR ((laser AND vapo*)) OR ((pvp AND prostat*)) OR ((pvp AND laser)), 33

(photo-selective vapo*) OR (photoselective vapo*), 17

((Moxy or Moxy*)) OR ((greenlight OR greenlight* OR XPS-greenlight OR greenlight-XPS* OR greenlight XPS* OR green light OR green-light)), 361

(Moxy or Moxy*), 0

(greenlight OR greenlight* OR XPS-greenlight OR greenlight-XPS* OR greenlight XPS* OR green light OR green-light), 361

((prostatic hyperplasia)[mh])[mh] OR (prostatic hyperplas*) OR (prostat* hyperplasia) OR (prostat* obstruction) OR ((prostat* adenoma) OR (prostat* adenomas)) OR ((BHP OR BPO OR BPE)), 96

Source: WHO ICTRP

Interface/URL: https://trialsearch.who.int/AdvSearch.aspx

Database coverage dates: from inception
Search date: 30/11/2021
Retrieved records: 66

Searched using the advanced interface. No time limits applied, recruitment status ALL

Search 1: intervention: (greenlight OR greenlight* OR XPS-greenlight OR greenlight-XPS* OR greenlight XPS* OR green light OR green-light) AND condition: prostat* retrieved 17 records. All downloaded for further assessment.

Search 2: intervention: vapo* AND prostat* retrieved 28 records. All downloaded for further assessment.

Search 3: condition: prostat* AND (hyperplas* OR enlarg* OR hypertroph*) AND Primary sponsor: Boston Scientific retrieved 10 records. All downloaded for further assessment.

Search 4: condition prostat* AND Intervention: (laser AND vapo*) retrieved 11 records. All downloaded for further assessment.

Source: ClinicalTrials.gov

Interface/URL: https://clinicaltrials.gov/ct2/search/advanced

Database coverage dates: from inception
Search date: 30/11/2021
Retrieved records: 35
Searched using the advanced interface. No time limits applied, recruitment status ALL

Search 1: Condition: Prostate Hyperplasia AND Intervention/Treatment: greenlight OR greenlight* OR XPS-greenlight OR greenlight-XPS OR "greenlight XPS" OR "green light" OR green-light.

Also searched for Prostatic Hyperplasia and Prostatic.

23 studies found and downloaded

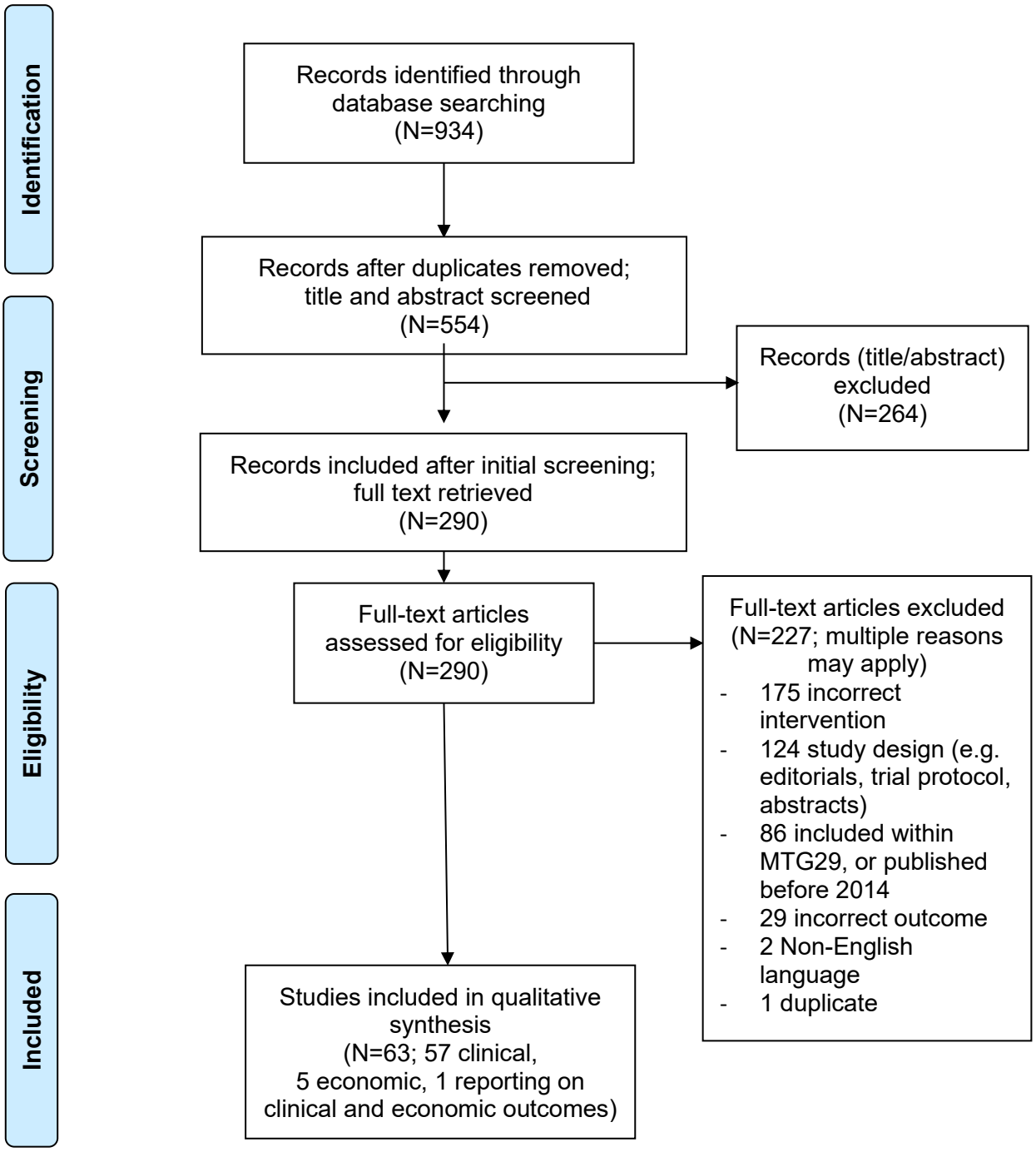
Search 2: Condition: Prostate Hyperplasia AND Sponsor/Collaborator: boston scientific

Also searched for Prostatic Hyperplasia and Prostatic.

12 studies found and downloaded

Appendix A3: PRISMA diagram illustrating EAC literature search

[From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097]



Appendix A4: Summary of studies included by the Company

		Company	EAC		
#	STUDY (author, paper, year)	Included	Included	Excluded	Reason(s) for exclusion
1	Abolazm *et al.* (J Urol 2020)	✓	✓		
2	Akhtar and Raina (J Lasers Med Sci 2018)	✓	✓		
3	Bajic *et al.* (Urolology 2019)	✓		✓	Intervention (Device power setting: 80 W vaporisation, 35 W coagulation, GreenLEP)
4	Barco-Castillo *et al.* (Neurourol Urodyn 2020)	✓	✓		
5	Brant *et al.* (Urology 2020)	✓		✓	Intervention (Power setting not reported)
6	Cacciamani *et al.* (Minerva Urol Nefrol 2019)	✓		✓	Study design (Systematic review, N=5 comparing GreenLight to TURP: Bachmann *et al.* 2013 (80 W); Capitan *et al.* 2011 (120 W); Horasanli *et al.* 2008 (80 W); Lukacs *et al.* 2012 (120 W); Xue *et al.* 2012 (120 W)
7	Campobasso *et al.* (J Endourol 2020)	✓	✓		
8	Castellani *et al.* (Res Rep Urol 2021)	✓		✓	Study design (systematic review, N=14 comparing GreenLight to TURP: Al-Ansari *et al.* 2010 (120 W); Kumar *et al.* 2016 (120 W); Purkait *et al.* 2017 (80 W); Ruskat *et al.* 2008 & Guo *et al.* 2015 (80 W); Tasci *et al.* 2008 (80 W); Telli *et al.* 2015 (120 W); Tugcu *et al.* 2008 (80 W); Bachmann *et al.* 2013 & Thomas *et al.* 2016 (80 W); Mordasini *et al.* 2018 (80 W); Pereira-Correia *et al.* 2011 (120 W); Xue *et al.* 2013 (120 W); Reimann *et al.* 2019 (180 W))
9	Castellucci *et al.* (Arch Ital Urol Androl 2020)	✓	✓		
10	Contreras *et al.* (J Endourol 2021)	✓	✓		
11	Culkin *et al.* (J Urol 2014)	✓		✓	Intervention (not GreenLight)
12	Destefanis *et al.* (World J Urol 2021)	✓	✓		
13	Elshal *et al.* (BJU Int 2020)	✓		✓	Intervention: GreenLight laser vapo-enucleation
14	Ferrari *et al.* (Minerva Urol Nephrol 2021a)	✓		✓	Intervention (en-bloc GreenLEP, Device power: 120 W vaporisation, 20 W coagulation)
15	Frendl *et al.* (J Urol 2021)	✓		✓	Intervention (photoselective vaporisation without specific reference to GreenLight, Device power not reported)
16	Gasmi *et al.* (World J Urol 2021)	✓	✓		
17	Ghahhari *et al.* (Surg Tech Int 2018)	✓	✓		
18	Ghahhari *et al.* (Eur Rev Med Pharmacol Sci 2021)	✓	✓		
19	Gilfrich *et al.* (J. Urol. 2021)	✓		✓	Intervention (photoselective vaporisation without specific reference to GreenLight, Device power not reported)
20	Gomez-Sancha *et al.* (World J Urol 2015)	✓		✓	Study design (narrative on enucleation procedure)
21	Gondran-Tellier *et al.* (J Endourol. 2021)	✓	✓		
22	Goueli *et al.* (J. Endourol. 2017)	✓	✓		
23	Gravas *et al.* (EAU Association of Urol, 2021)	✓		✓	Study design (EAU guidelines for LUTS and BPO)
24	Gu *et al.* (World J Urol 2020)	✓		✓	Study design (systematic review: comparison of GreenLight versus bipolar TURP: Peng *et al.* 2016 (80 W); Kumar *et al.* 2013 (120 W); Kumar *et al.* 2018 (120 W); Liu *et al.* 2014 (full text not available in English); Chimino *et al.* 2017 (180 W); comparison of GreenLight versus bipolar enucleation: Wang *et al.* 2017 (full text not available in English); Mu *et al.* 2017 (100-160 W)
25	Hibon *et al.* (Prog Urol 2017)	✓	✓		
26	Knoblauch *et al.* (Akuelle Urologie 2019)	✓		✓	Language (full text not available in English)
27	Kiba *et al.* (Res Rep Urol 2020)	✓		✓	Intervention (power setting 120 W)
28	Kini *et al.* (J Endourol 2020)	✓		✓	Intervention (power setting not defined)

		Company	EAC		
#	STUDY (author, paper, year)	Included	Included	Excluded	Reason(s) for exclusion
29	Kobayashi *et al.* (Low Urin. Tract Symptoms. 2021)	✓		✓	Intervention (power setting 120 W)
30	Laine-Caroff *et al.* (Int Urol Nephrol 2021)	✓		✓	Intervention (mixed power setting, 120 W used until 2011)
31	Lanchon *et al.* (Prog Urol 2018)	✓		✓	Comparator (open prostatectomy)
32	LaRussa *et al.* (J. Vasc Interv Radiol 2021)	✓		✓	Study design (systematic review, N=13: Bachmann *et al.* 2005 (power not specified); Bouchier-Hayes *et al.* 2010 (80 W); Bowen *et al.* 2013 (120 W); Capitan *et al.* 2011 (120 W); Horasanli *et al.* 2008 (80 W); Mithani *et al.* 2018 (Intervention: Biolitec laser); Mohanty *et al.* 2012 (80 W); Nomura *et al.* 2009 (80 W); Pereira-Correia *et al.* 2012 (120 W); Purkait *et al.* 2017 (80 W); Tasci *et al.* 2008 (power not specified); Thomas *et al.* 2016 (180 W), Tugcu *et al.* 2008 (power not specified))
33	Law *et al.* (World J Urol 2021)	✓	✓		
34	Leonardo *et al.* (Minerva Urol Nefrol 2020)	✓		✓	Study design (systematic review, N=1 using GreenLight: Skolarikos *et al.* 2008 (80 W, comparator open prostatectomy))
35	Liu *et al.* (Photobiomodul. Photomed Laser Surg 2020)	✓	✓		
36	Mattevi *et al.* (Arch Ital Urol Androl 2020)	✓	✓		
37	Meskawi *et al.* (World Urol 2017)	✓	✓		
38	Meskawi *et al.* (World J Urol 2019)	✓	✓		
39	Misrai *et al.* (J Endourol 2015)	✓		✓	GreenLEP Study design (video and abstract)
40	Misrai *et al.* (J Urol 2016)	✓		✓	Intervention (GreenLight PVP 120-180 W compared with GreenLEP 120 W)
41	Nguyen *et al.* (World J Urol 2020)	✓		✓	Study design (data pooled from 5 sources. GreenLight PVP from single study: Azizi *et al.* 2017 (180 W))
42	Nguyen *et al.* (World J Urol 2021)	✓		✓	Study design: subset of Law *et al.* 2021 (included)
43	Panthier *et al.* (World J Urol 2020)	✓		✓	Intervention (GreenLEP, 120 W)
44	Peng *et al.* (Lasers Med Sci 2020)	✓		✓	Study design (meta-analysis, N=6; Elmansy *et al.* 2010 (NR); Elmansy *et al.* 2012 (120 W); Elshal *et al.* 2014 (60-120 W); Jaeger *et al.* 2015 (120/180 W); Kim *et al.* 2016 (120 W); Sun *et al.* 2019 (120 W))
45	Pierce *et al.* (J Endourol 2021)	✓	✓		
46	Plata *et al.* (Neurourol Urodyn 2021)	✓	✓		
47	Prudhomme *et al.* (J Endourol 2020)	✓		✓	Intervention (power setting, HPS fibres 120 W)
48	Rapisarda *et al.* (Minerva Urol Nefrol 2019)	✓		✓	Study design (review, N=1, NICE guidance)
49	Reale *et al.* (Minerva Urol Nefrol 2020)	✓	✓		
50	Sachs *et al.* (Asian J Urol 2020)	✓		✓	Intervention (power setting: NR)
51	Salciccia *et al.* (J Endourol 2021)	✓		✓	Study design (systematic review, N=5; Osterberg *et al.* 2013 (120 W); Ben-Zvi *et al.* 2013 (120 W vs 180 W, including in original MTG29); Bowen *et al.* 2013 (120 W); Berquet *et al.* 2015 (180 W); Corbel *et al.* 2014 (180 W, full text not available in English))
52	Schwarz *et al.* (World J Urol 2021)	✓		✓	Study design (review)
53	Soans *et al.* (Aging Male 2020)	✓		✓	Study design (systematic review, N=2; Terrasa *et al.* 2013 (120 W); Elshal *et al.* 2012 (NR))
54	Stone *et al.* (J Endourol 2016)	✓		✓	Intervention (power setting: NR)
55	Sun *et al.* (Sci Rep 2019)	✓		✓	Intervention (power setting: 120 W)
56	Thoulouzan *et al.* (Prog Urol, 2017)	✓		✓	Language (full text not available in English)

		Company	EAC		
#	STUDY (author, paper, year)	Included	Included	Excluded	Reason(s) for exclusion
57	Trail *et al.* (J Endolum Endourol 2021)	✓	✓		
58	Trujillo *et al.* (J Endourol 2021)	✓	✓		
59	Valdivieso *et al.* (BJU Int 2018)	✓	✓		
60	Vanalderwerelt *et al.* (Low Urin Tract Symptoms 2021)	✓		✓	Intervention (mixed device and power setting: KTP 80 W, HPS 120 W, XPS 180 W)
61	Xu *et al.* (Lasers Med Sci 2021)	✓	✓		
62	Yoo *et al.* (World J Urol 2017)	✓		✓	Intervention (power setting: 120 W)
63	Yu *et al.* (Int Neurourol 2021)	✓		✓	Intervention (power setting: 80 W)
64	Zheng *et al.* (World J Urol 2019)	✓		✓	Study design (N=11; Ruszat *et al.* 2007 (80 W); Woo *et al.* 2008 (120 W); Karatas *et al.* 2010 (80 W); Chen *et al.* 2013 (120 W); Choi *et al.* 2013 (120 W); Shao *et al.* 2013 (120 W); Sohn *et al.* 2013 (120 W); Chen *et al.* 2013 (120 W); Lee *et al.* 2016 (180 W); Knapp *et al.* 2017 (180 W); Piotrowicz *et al.* 2018 (120 W))
65	Zhou *et al.* (Lasers Med Sci 2021)	✓		✓	Study design (meta-analysis, N=4; Kobayashi *et al.* 2020 (120 W); Guo *et al.* 2015 (120 W); Chiang *et al.* 2010 (120 W); Ruszat *et al.* 2009 (120 W))
	Total	**65**	**25**	**40**	

Appendix A5: Summary of identified systematic reviews (N=10)

	Author (journal, year)	Study design	Device used	Cacciamani *et al.* (2019) (Greenlight vs TURP, N=5)	Lai (2019) 15 RCTs, 7 non-RCTs (n=2665) †	Zheng *et al.* (2019) N=11	Gu *et al.* (2020) N=7	Leonardo *et al.* (2020) 9 RCTs¥ (Greenlight as intervention N=1, n=125)	Peng *et al.* (2020) N=6	Soans *et al.* (2020) N=2	Castellani *et al.* (2021) GreenLight N=14	LaRussa *et al.* (2021) PVP in N=13	Salciccia *et al.* (2021) N=5
1	Akhtar and Raina (J. Lasers Med. Sci. 2018)	PCS	180 W										
2	Al-Ansari *et al.* (Eur. Urol. 2010)	RCT	120 W		☒						☒		
3	Bachmann *et al.* (J. Urol. 2015)*	RCT	180 W		☒								
4	Bachmann *et al.* (Eur Urol. 2015)*	RCT	180 W	☒	☒								
5	Bachmann *et al.* (Eur. Urol. 2005)	PCS	Not specified		☒							☒	
6	Ben-Zivi *et al.* (Urol. 2013)	PCS	120 W vs 180 W										☒
7	Berquet *et al.* (Lasers in Surg. Med. 2015)	PCS	180 W										☒
8	Bouchier-Hayes *et al.* (BJU Int. 2010)	RCT	80 W		☒							☒	
9	Bowen *et al.* (Ont. Health. Technol. Assess. Ser. 2013)	PCS	120 W									☒	☒

	Author (journal, year)	Study design	Device used	Cacciamani *et al.* (2019) (Greenlight vs TURP, N=5)	Lai (2019) 15 RCTs, 7 non-RCTs (n=2665) †	Zheng *et al.* (2019) N=11	Gu *et al.* (2020) N=7	Leonardo *et al.* (2020) 9 RCTs¥ (Greenlight as intervention N=1, n=125)	Peng *et al.* (2020) N=6	Soans *et al.* (2020) N=2	Castellani *et al.* (2021) GreenLight N=14	LaRussa *et al.* (2021) PVP in N=13	Salciccia *et al.* (2021) N=5
10	Capitán *et al.* (Eur. Urol. 2011)	RCT	120 W	☒	☒							☒	
11	Chen *et al.* (BMC Urol 2013a)	PCS	120 W			☒							
12	Chen *et al.* (Lasers Med. Sci. 2013b)	RCS	120 W			☒							
13	Choi *et al.* (Prostate Int. 2013)	RCS	120 W										
14	Cimino *et al.* (Int. J. Impotence Res. 2017)	RCS	180 W				☒						
15	Corbel *et al.* (Progres en Urologie 2014)	PCS	180 W										☒
16	Elmansy *et al.* (J. Urol. 2010)	RCT	Not specified						☒				
17	Elmansy *et al.* (J. Urol. 2012)	RCT	120 W						☒				
18	Elshal *et al.* (Urol. 2012)	PCS	Not specified							☒			
19	Elshal *et al.* (J. Urol. 2014)	PCS	60-120 W						☒				
20	Guo *et al.* (Lasers Med. Sci. 2015)	PCS	80 W		☒						☒		
21	Horasanli *et al.* (Urol., 2008)	RCT	80 W	☒	☒							☒	
22	Jaeger *et al.* (BJU Int. 2015)	PCS	120/180 W						☒				
23	Karatas *et al.* (Int. Braz. J. Urol. 2010)	PCS	80 W			☒							
24	Kim *et al.* (PLoS One 2016)	RCS	120 W						☒				
25	Knapp *et al.* (BJU Int. 2017)	RCS	180 W			☒							
26	Kumar *et al.* (J. Endourol. 2013)	RCT	120 W		☒		☒						
27	Kumar *et al.* (Low. Urin. Tract Symptoms 2018)	RCT	120 W		☒		☒				☒		
28	Lee *et al.* (World J. Urol. 2016)	RCS	180 W			☒							
29	Liu *et al.* (J. Sichuan Univ. Med. Sci. Ed. 2014)	NKβ					☒						
30	Lukacs *et al.* (Eur. Urol. 2012)	RCT	120 W	☒	☒								
31	Mohanty *et al.* (Indian J. Urol. 2012)	RCT	80 W		☒							☒	
32	Mordasini *et al.* (Urol. 2018)	RCT	80 W		☒						☒		
33	Mu *et al.* (Asian J. Androl. 2017)	PCS	160-100W				☒						
34	Nomura *et al.* (Int. J. Urol. 2009)	PCS	80 W		☒							☒	
35	Osterberg *et al.* (Urol. 2013)	PCS	80 W										☒
36	Peng *et al.* (Urol. 2016)	RCT	80 W				☒						
37	Pereira-Correia *et al.* (BJU Int. 2012)	RCT	120 W		☒						☒	☒	
38	Piotrowicz *et al.* (Photomed. Laser Surg. 2018)	RCS	120 W			☒							
39	Purkait *et al.* (Turk. J. Urol. 2017)	PCS	80 W								☒	☒	
40	Reimann *et al.* (J. Clin. Med. 2019)	RCS	180 W								☒		
41	Ruszat *et al.* (Eur. Urol. 2007)	PCS	80 W			☒							
42	Ruszat *et al.* (BJU Int. 2008)	PCS	80 W		☒						☒		
43	Shao *et al.* (Clin. Interv. Aging 2013)	RCS	120 W			☒							
44	Skolarikos *et al.* (J. Endourol. 2008)	RCT	80 W					☒					
45	Sohn *et al.* (Korean J. Urol. 2011)	RCS	120 W			☒							
46	Sun *et al.* (Sci. Rep. 2019)	PCS	120 W						☒				
47	Tasci *et al.* (J. Endourol. 2008)	PCS	Not specified		☒						☒	☒	
48	Telli *et al.* (Ther. Adv. Urol. 2015)	RCT	120 W		☒						☒		
49	Terrasa *et al.* (J. Sex Med. 2013)	PCS	120 W							☒			

	Author (journal, year)	Study design	Device used	Cacciamani *et al.* (2019) (Greenlight vs TURP, N=5)	Lai (2019) 15 RCTs, 7 non-RCTs (n=2665) †	Zheng *et al.* (2019) N=11	Gu *et al.* (2020) N=7	Leonardo *et al.* (2020) 9 RCTs¥ (Greenlight as intervention N=1, n=125)	Peng *et al.* (2020) N=6	Soans *et al.* (2020) N=2	Castellani *et al.* (2021) GreenLight N=14	LaRussa *et al.* (2021) PVP in N=13	Salciccia *et al.* (2021) N=5
50	Thomas *et al.* (Eur Urol. 2016)*	RCT	180 W		☒							☒	
51	Tugcu *et al.* (J. Endourol. 2008)	PCS	Not specified		☒							☒	
52	Wang *et al.* (Chinese J. Urol. 2017)	NKβ					☒						
53	Woo *et al.* (Eur. Urol. Suppl. 2008)	PCS	120 W			☒							
54	Xue *et al.* (J. Xray Sci. Technol. 2013)	RCT	120 W	☒	☒						☒		
	Total number of included studies			**5**	**22**	**11**	**7**	**1**	**6**	**2**	**14**	**13**	**5**

*Publication relating to GOLIATH trial
βPublication in language other than English
Abbreviations: RCT, randomised controlled trial; PCT, prospective cohort study; RCT, retrospective cohort study; NK, not known.

Appendix B: Critical appraisal of clinical evidence

Appendix B1: RCTs (Cochrane Collaboration's tool for assessing risk of bias)

Abolazm *et al.*, 2020 (n=49 randomised to 2 arms; 46 with outcomes reported at 1 year)
First reviewer: KK; Second review: RP/RO

Bias domain	Source of bias	Support for Judgement	Review authors' judgement (assess as low, unclear, or high risk of bias)
Selection bias	Random sequence generation	Single-site study (assumed from author affiliation). "Patients were randomly allocated to 1 of the 2 groups in a 1:1 ratio using computer generated random tables."	Low risk
	Allocation concealment	"Eligible patients with LUTS secondary to BPO in whom medical treatment failed (persistent LUTS despite medical treatment for 3 months) were asked to participate in this trial." Unclear if consecutive patients. However patient demographics same between each arm (no significant differences in age at surgery, diabetes mellitus, Qmax, PVR, IPSS, QoL, PdetQmax, pre-op BOOI, pre-op prostate medication, pre-op phosphodiesterase type 5 inhibitors, pre-op anticholinergic drugs, pre-op PSA, pre-op TRUS prostate size).	Low risk
Performance bias	Blinding of participants and personnel*	Not possible to blind surgeons (unavoidable). "Patients and outcome assessors, including the nurses who performed uroflowmetry and the physician who performed the PFS [pressure flow study], were blinded to the nature of the procedure."	Low risk
Detection bias	Blinding of outcome assessment*	"The trial primary end point was the percent of preserved AE at 1 year in each group. The change in sexual function from baseline was assessed. Details of ejaculatory function were evaluated by the Ej-MSHQ. Furthermore, the change in the total IIEF-15 score and its subdomains from baseline to the postoperative score was determined and compared. Secondary outcomes included the degree of LUTS relief as assessed by the IPSS, Qmax, PVR and urodynamic end points, including	Low risk

Bias domain	Source of bias	Support for Judgement	Review authors' judgement (assess as low, unclear, or high risk of bias)
		PdetQmax and the BOOI. Furthermore, perioperative complications and the need for re-treatment were reported and compared." As per above, patients and those measuring uroflowmetry and pressure flow study were blinded.	
Attrition bias	Incomplete outcome data*	49 patients randomized; n=25 ejaculatory hood sparing GL-PVP, n=24 standard GL-PVP. Analysis at 1 year included n=24 and n=22 respectively. Reasons for exclusions reported in Fig 1: one patient in each arm lost to follow-up and one patient in standard GL-PVP arm withdrew consent and did not receive allocated intervention.	Low risk
Reporting bias	Selective reporting	Power calculation based on percent of preserved antegrade ejaculation evaluated using Ej-MSHQ (not listed as outcome of interest in NICE Final Scope, though implied in QoL). Primary and secondary outcomes listed in methods. Primary outcome measure results in Table 2 and Figure 3. Secondary outcome measures in Figure 4. Complications in each arm reported in Table 3, however study not powered to detect differences in these outcomes. Limitation acknowledged by study authors: small sample size (but adequately powered for primary endpoint, AE preservation), but note inclusion of urodynamic assessment seems to help provide more insight into the procedure related outcome.	Low risk
Other bias	Anything else, ideally pre-specified.	"No direct or indirect commercial, personal, academic, political, religious or ethical incentive is associated with publishing this article." No funding source identified for the work. No trial registration. Very specific eligibility criteria (which appears to differ from EUA: "sexual activity (continuous relationship with the same partner), an IPSS ≥15, BOOI ≥ 20 according to PFS and a TRUS estimate prostate size of 30 to 90 grams. Exclusion criteria were preoperative sexual dysfunction or EjD, a diagnosis of prostate cancer,	Low risk

Bias domain	Source of bias	Support for Judgement	Review authors' judgement (assess as low, unclear, or high risk of bias)
		neurological disorders and detrusor hypocontractitlity. Catheter dependent patients and patients with bladder stones were excluded from study due to inability to perform a baseline PFS." [Note associated editorial and reply by authors]	
*Assessments should be made for each main outcome or class of outcomes.			

Appendix B2: Non-randomised comparative evidence, assessed by the Joanna Briggs Institute Checklist for Quasi-Experimental Studies.

Cindolo *et al.* (2017)

First reviewer (KK), Second reviewer (RO)

Criteria	Yes	No	Unclear	N/A	EAC justification
1. Is it clear in the study what is the 'cause' and what is the 'effect' (i.e. there is no confusion about which variable comes first)?	✓				Included patients undergoing standard or anatomical PVP (cause) and following outcomes (effect) thereafter.
2. Were the participants included in any comparisons similar?		✓			No difference in age, baseline IPSS, or Qmax. Significant difference in prostate volume and baseline PSA.
3. Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?		✓			No significant difference in BPH or LUTS therapy, antiplatelet or anticoagulation therapy, catheter use, or use of anaesthesia during surgery between arms. Prophylactic antiobiotics administered to all patients. Number of fibres not reported, and significant difference in operative time, lasing time, energy used, and duration of follow up between arms.
4. Was there a control group?	✓				Standard PVP (control) versus anatomical PVP.
5. Were there multiple measurements of the outcome both pre and post the intervention/exposure?	✓				IPSS, Qmax, PSA, recorded at baseline and 6 months. Additional "last available" PSA also reported.
6. Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?		✓			"Median follow-up duration was 17.7 (12.0–25.8) months. The median follow-up duration was significantly shorter for patients who underwent aPVP (15.1 versus 18.8 months, p<0.001)." Risk of bias, although authors acknowledge their inability to observe longer term complications due to length of follow up.

7. Were the outcomes of participants included in any comparisons measured in the same way?			✓		Authors acknowledge "complications assessment and management (as re-intervention) may vary according to the different centers" but EAC considers it likely to be consistent across the same centre for patients undergoing standard PVP and aPVP. Additionally complications measured via Clavien-Dindo classification, standard IPSS, Qmax, PSA, and functional outcomes reported, and patient satisfaction measured using PGI-I.
8. Were outcomes measured in a reliable way?	✓				Standardised measures used, as above, and analysis retrospective.
9. Was appropriate statistical analysis used?	✓				Analysis conducted to adjust for follow-up duration (linear and quintiles, Table 3). Multivariable proportional odds regression model performed (included propensity scores).
Comment: Five authors declared honoraria for tutorship from AMS. No funding source reported. Authors acknowledge limitations of study, including: retrospective nature, non-randomised design, different surgical experience, pre- and post-operative management was not standardised, complication assessment and management may vary between centres, short follow-up, number of fibre used were partially available and thus excluded from analysis. Potential overlap with Castellani *et al.* (2018) and Castellucci *et al.* (2020), due to dates of recruitment, recruiting centres, and authorship; however unconfirmed.					
Overall appraisal					Include (fair quality)

Gondran-Tellier *et al.* (2021)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Unclear	N/A	EAC justification
1. Is it clear in the study what is the 'cause' and what is the 'effect' (i.e. there is no confusion about which variable comes first)?	✓				"The aim of this multi-institutional study was to evaluate the efficacy and safety of BPO surgery in patients with preoperative catheterization who failed TWOCs after AUR."
2. Were the participants included in any comparisons similar?	✓				Consecutive patients undergoing BPH between January 2017 and January 2019. The population included patients with refractory urinary retention despite the use of alpha-blocker and trial without catheter. All patients had preoperative urinary catheter. Patients known to have neurogenic bladder, prostate cancer, or urethral stricture were excluded from the analysis.
3. Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	✓				All patients were catheterised (retention), all tried alpha-blocker.
4. Was there a control group?	✓				Comparison TURP, PVP, endoscopic enucleation (GreenLEP and HOLEP combined), PAE, open prostatectomy
5. Were there multiple measurements of the outcome both pre and post the intervention/exposure?	✓				"All patients included had unsuccessful TWOC(s) and had a preoperative urinary catheter." Retreatments reported and stated explicitly.
6. Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?	✓				Through study inclusion criteria all followed to minimum of 12 months.

7. Were the outcomes of participants included in any comparisons measured in the same way?	✓				Complications categorised via Clavien-Dindo, duration of catheterisation.
8. Were outcomes measured in a reliable way?	✓				All arms reported 30 days complication, retreatment and catheter-free survival at 12 months.
9. Was appropriate statistical analysis used?		✓			Multivariate analysis included (backward stepwise, variables with $p<0.02$ in univariate analysis considered). Baseline characteristics not compared across arms – potential confounders.
Comment: The authors declare no financial interests. No funding was received for this article. Authors acknowledge limitations of study, including: retrospective design, short follow-up, lack of functional outcomes (IPSS, Qmax, PVR) as they were not available due to inclusion of patients with prolonged bladder catheterisation, did not include newer techniques (prostatic urethral lift, aquablation, water vapour thermal therapy).					
Overall appraisal					Include (fair quality)

Hibon *et al.* (2017)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Unclear	N/A	EAC justification
1. Is it clear in the study what is the 'cause' and what is the 'effect' (i.e. there is no confusion about which variable comes first)?	✓				"The purpose of this study was to compare the initial results after conventional vaporization versus anatomical vaporization."
2. Were the participants included in any comparisons similar?	✓				Patients undergoing PVP to treat large prostate (>80 cm^3 as measured by sonography). Patients with a non-sterile presurgical urine bacterial culture were excluded.
3. Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	✓				No difference in ASA category, foley catheterisation between arms, medical treatment of BPH, or antiagregant or anticoagulant treatment (Table 1)
4. Was there a control group?	✓				GreenLight PVP versus anatomical PVP.
5. Were there multiple measurements of the outcome both pre and post the intervention/exposure?	✓				IPSS, QoL (assumed to be IPSS-QoL although not explicitly stated), PVR, PSA, Qmax, prostate volume
6. Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?		✓			All patients completed follow up. Follow-up significantly different between arms (mean 9.3 versus 3.8 months, $p<0.001$)
7. Were the outcomes of participants included in any comparisons measured in the same way?	✓				Complications measured using Clavien-Dindo classification.
8. Were outcomes measured in a reliable way?		✓			Measured at different time points, no comparison with baseline within each arm.

9. Was appropriate statistical analysis used?		✓			Follow-up was significantly longer in Group 1 (GreenLight PVP) however this was not accounted for in analysis. No multi-variate analysis (to account for confounders), no subgroup analysis, no correction for multiples statistical tests. No comparison of number of patients in retention pre-operatively.
Comment: Two authors reported proctors for Boston-AMS, three authors declared no competing interests. No funding source reported. Authors acknowledge limitations of study including: large amount of missing data (due to method of data collection from medical records), short duration of follow-up, small sample size.					
Overall appraisal					Include (poor quality)

Mathieu *et al.* (2017)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Unclear	N/A	EAC justification
1. Is it clear in the study what is the 'cause' and what is the 'effect' (i.e. there is no confusion about which variable comes first)?	✓				Aim is to compare BPH treatments and outcomes thereafter. Data taken from database including nine French institutions.
2. Were the participants included in any comparisons similar?		✓			Age and ASA category, and urinary retention similar across arms. However prostate volume and antiplatelet/anticoagulation status was significantly different between arms (Table 2).
3. Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?		✓			Antiplatelet and anticoagulant use different across arms. BPH medication not reported across arms.
4. Was there a control group?		✓			4-way comparison (TURP, open prostatectomy, HoLEP/ThuLEP, PVP).
5. Were there multiple measurements of the outcome both pre and post the intervention/exposure?		✓			Study is reporting on operation time, LoS, and complications only. No comparison of efficacy.
6. Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?			✓		Readmissions reported, but duration of follow-up not recorded or compared between arms.
7. Were the outcomes of participants included in any comparisons measured in the same way?	✓				Complications recorded using Clavien-Dindo classification.
8. Were outcomes measured in a reliable way?	✓				Study is reporting on operation time, LoS, and complications only.

9. Was appropriate statistical analysis used?		✓			Multivariate analysis included. Cost analysis reported (device costs+consumables+mean LoS). Analysis separated for patients with prostate <80 g and ≥80 g.
Comment: Some authors declare support from AMS or Boston Scientific. No funding source reported. Authors acknowledge limitations of study, including: exclusion of readmission costs in cost analysis, retrospective nature, surgeon skill and experience in procedures was not available, learning curve may have biased results. Mixture of public (N=7) and private (N=2) centres, with a different number of BPH surgeries (different experience), and different breakdown of mTURP, open prostatectomy, GreenLight PVP, HoLEP/ThuLEP practice.					
Overall appraisal					Include (poor quality)

Mattevi *et al.* (2020)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Unclear	N/A	EAC justification
1. Is it clear in the study what is the 'cause' and what is the 'effect' (i.e. there is no confusion about which variable comes first)?	✓				"In the present study, we report our experience with photoselective vaporization of the prostate (PVP) and TURP regarding complications and functional results with a follow up to 1 year."
2. Were the participants included in any comparisons similar?	✓				Consecutive patients undergoing surgical treatment of BPH between March 2015 and March 2016 at a single centre in Italy. Discussion states that the latest 50 were used (although not described in methods).
3. Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	✓				No difference in anticoagulation, ASA score, operative time, between arms (Table 1).
4. Was there a control group?	✓				TURP assumes standard of care.
5. Were there multiple measurements of the outcome both pre and post the intervention/exposure?	✓				Qmax, IPSS and PSA measured pre-operatively and at 1 year and compared across arms (Table 3).
6. Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?			✓		Length of follow-up not reported. Methods state followed up to 1 year (but no comparison of median duration between arms).
7. Were the outcomes of participants included in any comparisons measured in the same way?	✓				Complications measured using Clavien-Dindo classification.

8. Were outcomes measured in a reliable way?	✓				Early complications within 30 days, late complications within 90 days, reoperation within 1 year.
9. Was appropriate statistical analysis used?		✓			No multi-variate analysis (to account for confounders), no subgroup analysis, no correction for multiples statistical tests. No comparison of number of patients in retention pre-operatively.
Comment: Authors declared no conflicts of interest. Funding source not reported. Authors acknowledge limitations of the study including: non-randomised design (authors state that patients can be unwilling to be randomised), small number (however authors state that age, prostate volume, use of antiplatelets/anticoagulants and ASA score were similar between arms).					
Overall appraisal					Include (fair quality)

Mesnard *et al.* (2021)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Unclear	N/A	EAC justification
1. Is it clear in the study what is the 'cause' and what is the 'effect' (i.e. there is no confusion about which variable comes first)?	✓				"The main objective of our study was to evaluate the post-operative morbidity of oncological and BPH prostate surgeries and interventions in patients with haemophilia A and haemophilia B."
2. Were the participants included in any comparisons similar?			✓		All patients have haemophilia A and B and underwent prostate interventions between 1st January 1997 and 1st September 2020. However unclear of how many each type had TURP or GreenLight (proportion of each not reported). Only patients with mild haemophilia included.
3. Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?			✓		One patient (TURP) treated with 3 infusions of desmopressin, 4 patients treated with rFVIII however unclear which group these were in (TURP or GreenLight PVP). Additional treatments during hospitalisation, however poorly reported across TURP and GreenLight arms.
4. Was there a control group?	✓				Comparison of TURP and GreenLight PVP
5. Were there multiple measurements of the outcome both pre and post the intervention/exposure?		✓			No repeated measurements
6. Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?	✓				Intrinsic to eligible criteria, all patients minimum of 30 days post-op follow-up, however maximum follow-up not reported.
7. Were the outcomes of participants included in any comparisons	✓				Complications recorded using Clavien-Dindo classification.

measured in the same way?					
8. Were outcomes measured in a reliable way?		✓			Retrospective exhaustive extraction from medical records (potential for missed events outwith hospital care). No reporting of length of follow-up in each arm. Outcomes and characteristics poorly reported across arms.
9. Was appropriate statistical analysis used?	✓				Lack of statistical analysis is appropriate due to small numbers in each arm (n=5 TURP, n=5 GreenLight PVP).
Comment: Authors declare no conflict of interest. No funding source reported. Authors acknowledge limitations of study including: retrospective nature, patient groups so small unable to conduct statistical comparisons, results cannot be generalised to patients with moderate or severe haemophilia.					
Overall appraisal					Include (poor quality)

Reimann *et al.* (2018)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Unclear	N/A	EAC justification
1. Is it clear in the study what is the 'cause' and what is the 'effect' (i.e. there is no confusion about which variable comes first)?	✓				Cause: BPH surgery. Effect: symptoms "The primary intention of this study was to evaluate the progression of GL-XPS in a high volume center for GL-XPS with the primary outcome measurements of operation and laser time with regard to prostate volume and year of surgery as specific parameters of experience"
2. Were the participants included in any comparisons similar?	✓				All patients undergoing for surgery for BPH symmptoms between June 2010 and Feb 2015 at a single centre via type types of surgery (PVP or TURP). Only patients with participated in post-operative follow up included (unclear how patient deaths handled, reasons for exclusion not explicitly reported – potential source of bias).
3. Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	✓				BPH clinical care pathway.
4. Was there a control group?	✓				PVP versus TURP (authors describe TURP as gold standard in BPH treatment but

					with several known complications *e.g.* bleeding)
5. Were there multiple measurements of the outcome both pre and post the intervention/exposure?	✓				Change in IPSS-QoL, but length of follow up different in PVP (median 27 months) and TURP arms (median 36 months) potential source of bias.
6. Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?	✓				Assuming from eligibility criteria that follow-up completed for all included patients (however no flow diagram to confirm). Length of follow-up different across arms.
7. Were the outcomes of participants included in any comparisons measured in the same way?	✓				Same measurements applied to both. Different follow-up.
8. Were outcomes measured in a reliable way?		✓			Long-term follow-up reported at 27 months for GreenLight PVP and 36 months for TURP – unfair comparison. No raw data for IPSS-QoL shared. No comparison of IPSS, Qmax, PSA reported.
9. Was appropriate statistical analysis used?		✓			No multivariate analysis, no correction for multiple statistical tests.
Comment: Authors state perioperative antibiotic prophylaxis was significantly higher in PVP group than TURP (83% versus 32%, p<0.001) which may confound results. IPSS and continuing aspirin until operation were different between groups at baseline (Table 1). Authors acknowledge limitations incuding: retrospective design, lack of systematic follow-up, assumptions regarding surgical technique and experience. One author receives honoraria as a consultant/proctor for Boston Scientific, all other authors declare no conflict of interest. Funding for the work not declared.					
Overall appraisal					Include (poor quality)

Appendix B3: Observational studies, assessment using the NIH National Heart, Ling and Blood Institute Cohort tool.

Aboutaleb *et al.* (2018)
First reviewer (KK), Second reviewer (RO)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			[Abstract]: "Our objectives were to evaluate the efficiency of transurethral bipolar plasma vaporisation of the prostate (BPVP) using the button electrode and compare it to green laser vaporisation of the prostate (GLVP)."
2. Was the study population clearly specified and defined?	✓			Patients with BPO enrolled between March 2012 and January 2017. Inclusion and exclusion criteria also well defined.
3. Was the participation rate of eligible persons at least 50%?			✓	No patient flow reported.
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	✓			Inclusion criteria: age >50 years, prostate volume 30-100 ml, serum PSA <2.5 ng/ml, IPSS ≥20, Qmax ≤ 10ml/s and failed medical therapy for BPH. Exclusion criteria: abnormal digital rectal exam or ultrasonography with suspicion of prostate cancer, history of prostate cancer, previous urethral or prostate surgery, urethral stricture, neurogenic bladder, bladder neck sclerosis, bladder calculi, BPH-related hydronephrosis, active urinary tract infections, renal insufficienct, previous myocardial infarction within 6 monhts, previous TURP, serum creatinine >200 mol/l.
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification provided (likely pragmatic).
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Retrospective study. All patients undergoing vaporisation and outcomes reported. No trial registration.
7. Was the timeframe sufficient so that one could reasonably expect to see an association			✓	Sufficient in terms of intra-operative safety and short term complications, unclear if differences in IPSS, QoL, PVR will be sustained longer term.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
between exposure and outcome if it existed?				
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?			✓	N/A
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?		✓		Surgical techniques fully described, so assumed to have been implemented consistently. Only operative time reported (not different between groups).
10. Was the exposure(s) assessed more than once over time?		✓		No reoperation reported, and would not be expected in the short timeframe of the study.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?		✓		Complications not reported using Clavien-Dindo, and therefore not clearly defined. IPSS, QoL (assumed IPSS-QoL), Qmax, Qave, PVR reported at 3 months. Unclear whether implemented consistently across all participants.
12. Were the outcome assessors blinded to the exposure status of participants?		✓		No blinding reported, but unlikely due to being retrospective study.
13. Was loss to follow-up after baseline 20% or less?	✓			From Table 4, assume all patients followed to 3 months.
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?		✓		No multivariate analysis applied, no correction for multiple statistical tests.
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	One author declared employee of University and received grants from ethics committee. Research received no specific grant from any funding agency in the public, commercial or not-for-profit sector. Authors acknowledge short follow-up as main limitation, along			

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
	with absence of cost comparison of two techniques. Include as single arm only (comparator out of scope).			
Quality Rating	Poor			

Azizi *et al.* (2017)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"To compare perioperative parameters, safety and short-term functional outcomes between GreenLight 180 W-XPS photo-selective vaporization of the prostate (PVP) and vapor-incision technique (VIT)."
2. Was the study population clearly specified and defined?	✓			Retrospective LUTS secondary to BPH treated with laser prostatectomy using GreenLight XPS-180 W between August 2010 and August 2014. 5 centres in Canada and US. Surgical indications by AUA and CUA guidelines.
3. Was the participation rate of eligible persons at least 50%?		✓		No - 444/956 patients included after propensity matching. [Baseline characteristic comparisons of the 672 PVP and 284 vapoincision in Table 1]
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	✓			Same inclusion criteria applied to all. Difference in PSA between propensity matched arms, rest variables the same. No trial registration.
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification as to number of patients (likely pragmatic, all patients recruited during the same period).
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Cohort selected on basis of treatment (GreenLight) surgical preference determined subgroups but analysed retrospectively (no influence). No trial registration reported.
7. Was the timeframe sufficient so that one could reasonably expect to see an association		✓		6 months, possibly too short for medium and long term efficacy outcomes, too short for reintervention outcomes.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
between exposure and outcome if it existed?				
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?	✓			Laser time, operative time and energy used compared between intervention and comparator exposures.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Mean operative time, mean laser time, mean energy, and fibres used recorded in both arms.
10. Was the exposure(s) assessed more than once over time?			✓	Reintervention and retreatment with same procedure not reported and not applicable to study design.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			IPSS, Qmax, PVR all standard outcomes. Complications using Clavien-Dindo grade. Assume IPSS-QoL used (but not explicitly reported).
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No mention of blinding.
13. Was loss to follow-up after baseline 20% or less?			✓	Follow-up completion not reported.
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?		✓		No multivariate analysis reported.
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	Conflicts of interest and funding are not reported in the paper. The authors acknowledge some limitations of the study: possible selection bias towards vapor-resection in patients with large prostates (>80 ml), lack of cost evaluation, longer follow-up required to assess functional outcomes and retreatment rates.			

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
Quality Rating	Fair			

Berquet *et al.* (2015)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"The objective of this study was to prospectively evaluate the feasibility, safety, and efficacy of ambulatory PVP with the Greenlight 1 laser 180 W-XPS."
2. Was the study population clearly specified and defined?	✓			All consecutive patients undergoing GreenLight PVP at two French centres between May 2012 and June 2013. Indications based on EAU guidelines or French Association of Urology. Exclusion criteria stated.
3. Was the participation rate of eligible persons at least 50%?	✓			All consecutive.
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	✓			Eligibility criteria applied to all. Subjects recruited during same time period (May 2012 – June 2013).
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification provided (assumed pragmatic all patients between specified time period)
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Cohort defined through use of GreenLight PVP using XPS 180 W. No trial registration reported.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?			✓	Safety up to 30 days, efficacy up to 3 months, however mean follow-up reported as 9 month (unclear)
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the	✓			Assume all 180 W. Laser time, operative time, energy used reported across subgroups based on prostate volume (≤40

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?				ml, 41-79 ml and ≥80 ml) as well as overall cohort with p values.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Lasing time, mean energy supplied, total energy reported.
10. Was the exposure(s) assessed more than once over time?			✓	Not reported, short term follow up.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Mean follow-up 9 months, functional outcomes standard: Qmax, PVR, IPSS, IPSS-QoL.
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No mention of blinding
13. Was loss to follow-up after baseline 20% or less?			✓	Not reported no data flow diagram, assume 3 month follow-up achieved in all patients.
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	✓			A multivariable logistic regression model was used to identify predictive factors of complications including covariates with a P-value<0.05 in univariable analysis.
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	Unclear is all outcomes recorded for all patients (denominator not reported, *e.g.* Fig1 adds to 100). P-value[2] unclear in Table 4. Selection bias in that patients were selected for ambulatory care (may be low risk patients). Authors acknowledge potential learning curve. Includes private and public hospital setting (may not be fully generalisable to NHS). Conflict: One author is a proctor for AMS.			
Quality Rating	**Fair**			

Campobasso *et al.* (2020)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"We decided to analyze a large multicenter cohort of 1031 patients to evaluate complication rates and functional outcomes in patients with BPO treated by 180 W LBO laser according to prostate volume."
2. Was the study population clearly specified and defined?	✓			Retrospective review of standard and anatomical PVP in multi-institutional prospective database between September 2011 and October 2017 using 180 W GreenLight. Exclusion criteria explicitly stated. Note: GreenLEP excluded, but reference to enucleation in methods.
3. Was the participation rate of eligible persons at least 50%?			✓	Not reported, assume all in database eligible by definition of inclusion.
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	✓			Database for inclusion with same criteria applied to cohort. Subjects recruited during same time period.
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		Not justified (though assumed pragmatic, all patients attending within defined dates).
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Cohort defined through use of GreenLight intervention. No trial registration reported.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	✓			Minimum follow-up duration 12 months, patients with prostates ≥100 ml had longer follow-up periods (16.5 – 35.0 months) compared to those with prostates <100 ml (12.0 – 24.0

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
				months). Functional outcomes and complications evaluated over follow-up time.
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?	✓			Lasing time, operative time and energy used reported across full cohort and by pre-operative prostate volume (<100 ml, ≥100 ml). Power settings not reported.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			180 W, surgical technique, operative time, lasing time, energy used reported.
10. Was the exposure(s) assessed more than once over time?	✓			Reintervention (TURP, Bladder neck incision, urethrotomy) reported. GreenLight PVP was not performed more than once.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			IPSS, Qmax, complications via Clavien-Dindo all standard reporting. Timing of PGI-I not explicitly reported but assumed short term.
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No mention of blinding.
13. Was loss to follow-up after baseline 20% or less?	✓			Median (IQR) follow-up 17.0 (12.0 to 25.3) months, “All the patients were recalled and underwent an outpatient clinic evaluation at least after 3, 6, and 12 months and then annually”
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	✓			No multi-variate analysis, no correct for multiple statistical tests (just multiple paired t-tests applied).
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	Several authors do surgical tutorship for AMS and receive honoraria. No funding received. Authors acknowledge limitations: retrospective design, several surgeons with different levels of experience, heterogeneity of centres to report and manage pre-			

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
	and post-operative events, lacking reporting on number of fibres used. Good reporting of subgroups (n=916 with <100ml; n=115 with ≥100ml).			
Quality Rating	**Good**			

Castellani *et al.* (2018)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"The aim of this study is to compare data on efficacy and safety of patients undergoing in a daily practice standard 180-Watt GreenLight laser PVP as compared to ThuVEP."
2. Was the study population clearly specified and defined?	✓			Patients having surgery for BPH at 4 centres (3 GreenLight, 1 ThuLEP) between 2014 and 2017, indications for surgery following EAU guidelines."Exclusion criteria were neurologic disease, history of prostate cancer or previous urethral stricture or prostate surgery. Men who underwent concomitant surgical procedures (urethrotomy, cystolithotripsy, transurethral resection of incidental bladder tumor, and so on) were also excluded. Suspicious prostate cancer was ruled out preoperatively with prostate biopsy."
3. Was the participation rate of eligible persons at least 50%?		✓		Total of 291 PVP, 214 ThuVEP. Only 93 PVP and 158 ThuVEP at 12 months. This was then used for propensity matching resulting in 45 in each arm. High risk of bias.
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified		✓		GreenLight PVP conducted in 3 centres, ThuVEP conducted in a different single centre. Patients recruited during same time period. High risk of bias.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
and applied uniformly to all participants?				
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification (like pragmatic within study time frame, study only included patients with complete follow-up data).
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Retrospective analysis of data collection of men undergoing BPH surgery. No trial registration reported.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?		✓		Intraoperative complications. Reoperations captured within 30 days too short. Changes in IPSS, Qmax and reoperation may require longer follow-up than 1 year.
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?		✓		Surgical time is the only variable reported; energy used and laser time not reported relating to outcomes.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			No difference in total surgical time (min), antiplatelet/anticoagulation status and indwelling catheter history between arms after propensity matching.
10. Was the exposure(s) assessed more than once over time?	✓			Reoperations captured within 30 days, but type missing.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?		✓		Intra-operative complications categorised using Clavien-Dindo classification. Change in IPSS and Qmax treated as binary variables with threshold applied at 6 and 12 months different.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
12. Were the outcome assessors blinded to the exposure status of participants?		✓		No blinding reported.
13. Was loss to follow-up after baseline 20% or less?	✓			Through eligibility criteria those with missing 12 month follow-up excluded.
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?		✓		Multivariate analysis conducted, reporting that surgical technique is not predictive of patients' satisfaction and reoperation after 30 days, even after propensity matching. Authors state that the results the same for 12 month analysis (however not included in supplementary material). Cannot adjust for different centre conducting ThuVEP.
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	One author declared receipt of honoraria for tutorship from AMS. Other authors declared no conflict. Financial disclosures: none. Authors acknowledge limitations of study, including: small number of patients on antiplatelet/anticoagulant therapies in each arm (therefore unable to conduct statistical analysis), retrospective nature, non-randomised design, different surgical experience of user, preoperative and postoperative management not standardised, complication assessment and management different between centres, energy delivered not available in majority of cases, length and heterogeneity of follow-up. Propensity matching attempts to account for some heterogeneity in patient characteristics between arms, but is unable to account for these systematic/setting differences between arms. Potential overlap with Castellucci *et al.* (2020) due to dates of study inclusion, hospitals involved and authorship, but unconfirmed.			
Quality Rating	**Poor**			

Castellucci *et al.* (2020)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"The aim of this study is to evaluate the safety and feasibility of GreenLight 180 W XPS PVP combined with other surgical procedures. Moreover, we aim to test the effect of simultaneous procedure on perioperative outcomes, functional outcomes and complication rates."
2. Was the study population clearly specified and defined?	✓			PVP performed to relieve LUTS/BPH symptoms, extracted from multi-institutional database (2011-2016). Patients stratified by presence of concomitant procedure during same surgical session.
3. Was the participation rate of eligible persons at least 50%?			✓CD	Exclusions not reported (no data flow diagram)
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	✓			Retrospective extraction from database (no exclusion criteria listed), assume all included. Patients recruited from the same time period.
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification but likely pragmatic (all GreenLight PVP conducted within timeframe).
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Retrospective database. No trial registration reported.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	✓			Median follow-up of 17 months. Follow-up statistically different between subgroups, potential risk of bias.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?	✓			Energy used and laser time reported for full cohort and subgroups (PVP, PVP with concomitant procedure) with p values, number of patients with missing data also reported.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Concomitant procedures listed in table 1 (vescical lithotripsy, internal urethrotomy, TURB, vescical botulinum, inguinal hernia repair, colecistectomy, hydrocelectomy, laparoscopic bladder diverticulectomy). Laser time, energy used reported in both subgroups and statistically compared (no difference).
10. Was the exposure(s) assessed more than once over time?		✓		Re-intervention reported but duration and type not reported.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?		✓		Complications via Clavien-Dindo category, functional outcomes Qmax and IPSS. Total early and late complications not reported. Timing of events not reported.
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No blinding reported (retrospective analysis of database).
13. Was loss to follow-up after baseline 20% or less?			✓	Median follow-up of 17 months, however not explicitly reported how many patients were followed to 1 year, 2 years, and so on. No patient flow diagram.
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?		✓		Multivariate analysis conducted adjusting for prostate volume and age. No mention of anticoagulation in baseline characteristics or in outcomes analysis. Baseline characteristics show that duration of follow-up was different between subgroups

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
				(18 vs. 14.5 months, p<0.001) and history of catheterisation (21.2% versus 36.2%, p=0.02) which may explain difference in outcomes.
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	Conflicts and funding source not included in paper. Authors acknowledge limitations of study: retrospective nature, variation in surgical experience could not be controlled, non-standardised pre- and post-operative patient management, variation in assessment and management of complications across centres. Small number in concomitant procedure arm.			
Quality Rating	**Poor**			

Cimino *et al.* (2017)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"The aim of this study is to compare PVP vs TURP in terms of the BPH6 end point."
2. Was the study population clearly specified and defined?	✓			Eligibility criteria listed in Suppl Table 2. Additional exclusions: prostate cancer, neurogenic bladder disease or neurological disorders, patients with indwelling catheter.
3. Was the participation rate of eligible persons at least 50%?	✓			220 consecutive patients, 110 included (55 TURP, 55 GreenLight) [Baseline characteristic comparisons of the 101 TURP and 113 PVP in Suppl Table 1]. Number of eligible patients declining participation across pre-propensity-matched groups not reported.
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	✓			Suppl Table 2 applied to all. Comparison of baseline characteristics in Table 1 (paper states "no statistically significant differences for all variables" but no p-values reported). No trial registration. Patients recruited between same period (Jan 2014 – Jan 2016).
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification as to number of patients (likely pragmatic, all patients between Jan 2014 and Jan 2016).
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Cohort selected on basis of treatment (PVP or TURP), cohort followed forward in time. No trial registration reported.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between	✓			1 year follow-up.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
exposure and outcome if it existed?				
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?			✓	Not reported.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			✓	Power setting, total energy applied, duration not reported.
10. Was the exposure(s) assessed more than once over time?			✓	Not reported.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			BPH6 recovery as composite of 6 elements. Qmax, IPSS, SHIM scores used across groups. Unclear how safety captured (given 55 patients in each arm); reporting in Table 3 unclear.
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No mention of blinding.
13. Was loss to follow-up after baseline 20% or less?			✓	Assume all measurements available on all patients (not stated otherwise).
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	✓			Propensity scores computed by logistic regression. The multivariate logistic regression analysis, adjusted for preoperative variables, showed that PVP was independently associated with BPH6 end point (odds ratio = 3.77 (95% confidence interval 1.64–8.70); p<0.01).
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	Non-randomised design; attempted to address in propensity matching, however other factors may have contributed to choice of PVP, TURP not			

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
	included in baseline characteristics (medication, duration of symptoms etc). No significant difference in IPSS, peak flow, SHIM between TURP and PVP pre-op, 3, 6, 12 months. The authors declare no conflict of interest.			
Quality Rating	**Good**			

Chen and Chiang (2016)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"The purpose of this study was to evaluate the operative efficacy and safety of the GreenLight 180-W XPS laser system in comparison to the GreenLight 120-W HPS system"
2. Was the study population clearly specified and defined?	✓			Data were retrospectively collected from patients with lower urinary tract symptoms secondary to BPH undergoing treatment with the GreenLight 120-W HPS system (August 2008-September 2009) or 180-W XPS system (September 2014-September 2015) by a single surgeon."
3. Was the participation rate of eligible persons at least 50%?			✓	Patient flow not reported. Retrospective database review.
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	✓			All patients included had a poor response to alpha-blocker or 5ARI, indications for surgery in line with European guidelines. Exclusion criteria included prior urethral surgery, suspected neurogenic bladder and prostate cancer.
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification provided, likely pragmatic due to retrospective review.
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Retrospective database. No trial registration.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	✓			IPSS, Qmax, PVR and QoL reported at baseline, 1-6 month, 7-12 months. Up to 12 months follow-up for redo surgery (but unclear how many reached 12 months). Median follow-up not reported.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?	✓			Energy used, lasing time and number of fibres used reported across both groups in Table 1 with p values.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Applied energy, lasing time and number of fibres used reported.
10. Was the exposure(s) assessed more than once over time?	✓			"At 12-month follow-up, no one required redo TURP or photoselective vaporization of the prostate for residual prostatic tissue or regrowth of prostatic tissue in the XPS group, but one case (prostate size: 80 mL) in the HPS group."
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?		✓		Complications not reported using Clavien-Dindo classification. IPSS, Qmax, PVR and QoL (assumed IPSS-QoL) reported).
12. Were the outcome assessors blinded to the exposure status of participants?		✓		No blinding reported.
13. Was loss to follow-up after baseline 20% or less?			✓	Follow-up duration not reported. However clinical outcomes in Table 2 suggest follow-up not complete in all patients.
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?		✓		No multivariate analysis, no correction for multiple testing.
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	Authors declare no conflicts of interest, and confirmed no funding received for the work described in the article. Authors acknowledge limitations of study, including: retrospective nature, non-randomised design, small sample size, short			

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
	follow-up period, single surgeon, different time period for HPS group. Comparator out of scope, treat as single arm study.			
Quality Rating	Poor			

Eken and Soyupak (2018)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"Objective: To evaluate the safety and efficacy of the 180-W GreenLight XPS laser system for the treatment of benign prostatic hyperplasia in patients taking oral anticoagulants."
2. Was the study population clearly specified and defined?	✓			Consecutive patients undergoing PVP GreenLight XPS 180 W for treatment of LUTS associated with BPH between November 2012 and October 2016.
3. Was the participation rate of eligible persons at least 50%?			✓	No patient flow diagram provided. Assumed all eligible patients included; "informed consent was waived because this study involved analysis of existing medical records."
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	✓			Consecutive patients with same inclusion/exclusion defined criteria. Recruited during same time period.
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification provided (likely pragmatic).
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Retrospective analysis of patient undergoing GreenLight PVP. No trial registration.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?		✓		Short term (only 3 months) reasonable for safety but not efficacy.
8. For exposures that can vary in amount or level, did the study examine different levels of the		✓		Perioperative outcomes (operation time, laser time,

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?				energy used) reported as full cohort and not in subgroups.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Operating time, laser time, energy usage reported.
10. Was the exposure(s) assessed more than once over time?		✓		Reoperation reported (Table 4) but type of reoperation not reported. Subgrouped by anticoagulation status (dose, duration of use not reported). Also unclear how many taking each type of anticoagulation; "The anticoagulation group comprised 73 (31.3%) patients who used aspirin, 11 (4.7%) who used clopidogrel, and 9 (3.8%) who used warfarin sodium." Patient numbers do not add to 59, the percentages do not add to 100%. Anticoagulation arm also includes aspirin and clopidogrel.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?		✓		Complications not reported used Clavien-Dindo categories. IPSS, Qmax, PVR, PSA all standard outcomes.
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No mention of blinding.
13. Was loss to follow-up after baseline 20% or less?	✓			Short follow-up, 224/233 (96%) available at 3 months. Reasons for missing data: 3 converted to TURP (assume not followed), 2 moved to another city, 1 died of a condition unrelated to the surgery, 3 absent from follow-up visit for unknown reasons.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?		✓		No multivariate analysis, no paired analysis for IPSS, Qmax and PVR. No correction for multiple statistical comparisons.
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	The authors declared no conflicts of interest. No specific funding was received. The authors acknowledge limitations of the study including: short follow-up, and lack of recording sexual function at baseline or follow-up (however limitation of study design using existing medical notes). Study reports on prostate volume change during 3 months follow-up.			
Quality Rating	Poor			

Ferrari *et al.* (2021b)
First reviewer (RP), Second reviewer (KK)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"Objective: To analyse the chemical composition of the surgical smoke and the outflow irrigation fluid produced during a common endourological surgical procedure to treat benign prostatic obstruction (BPO)."
2. Was the study population clearly specified and defined?	✓			Prospective study, patients undergoing GreenLight PVP between July and September 2019, all patients provided written informed consent and recruited from a single site. Inclusion and exclusion criteria defined. Uncertainty regarding consecutive recruitment.
3. Was the participation rate of eligible persons at least 50%?			✓	Not reported. No patient flow diagram provided. Results state that ten patients were enrolled during the study.
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?			✓	Patients provided written consent with clearly defined inclusion/exclusion criteria. Recruited during same time period. 5 patients were recruited for gas sampling, 5 patients recruited for outflow fluid sampling; patient allocation method not reported.
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification provided, small sample size (n=10) from a single centre; recruitment likely pragmatic.
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Gas and outflow fluid samples collected at time of patient undergoing GreenLight PVP procedure. No trial registration.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	✓			Short-term analysis of samples taken during a procedure, exploratory aims to identify chemical compostion of gas and fluid associated with a

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
				standard procedure. Reasonable for safety and study design/aims.
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?		✓		Perioperative outcomes (operation time and energy used) reported as full cohort and not in subgroups.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Operating time and energy usage reported. Samples taken within similar time frames; gases collected at 1.2 l/min, outflow fluids collected “after approximately 15 to 20 minutes of laser activity”.
10. Was the exposure(s) assessed more than once over time?		✓		Samples were taken once at a single time point during procedure. Reoperation rates not reported, however this is considered as appropriate given the study aims.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			All samples were sent to a laboratory for analysis in clearly defined conditions.
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No mention of blinding. Assuming not possible as samples collected by surgical team and samples analysed under well-defined conditions.
13. Was loss to follow-up after baseline 20% or less?			✓	Short-term follow up, sample collected at time of procedure with no follow-up, considered not applicable.
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?			✓	No statistical analysis performed. Qualitative search of potentially toxic substances study design.
*CD, cannot determine; NA, not applicable; NR, not reported				

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
Comment	Three authors are consultants and proctors for Boston Scientific for GreenLight (manufacturer). Funding not reported. The authors acknowledge several limitations; not all gases produced during surgery could be analysed due to a lack of available standard available for all gases, gases collected by air pump so some gases may have dispersed in the operating room air, and analyses focussed on qualitative search of potentially toxic substances.			
Quality Rating	Fair			

Gasmi *et al.* (2021)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"The purpose of this study was to compare the perioperative and functional outcomes between GreenLight PVP and GreenLEP for the surgical management of benign prostatic obstruction with glands less than 100 mL."
2. Was the study population clearly specified and defined?	✓			Consecutive patients diagnosed with LUTS due to BPO who underwent GreenLight laser (PVP or GreenLEP) between April 2011 and April 2020. Exclusion criteria clearly defined.
3. Was the participation rate of eligible persons at least 50%?			✓	No data flow diagram, eligibility not reported, retrospective review.
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	✓			Data base for inclusion. Included patients from the same eligibility criteria and time period.
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification (assume pragmatic, as many patients as entered into database within a specified timeframe).
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Prospective database. No trial registration reported.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	✓			Median follow-up 14 months for PVP. Outcomes reported at 3 months and final follow-up.
8. For exposures that can vary in amount or level, did the study	✓			Comparison of 180 W PVP versus 120 W GreenLEP (out

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?				of scope). Laser time, energy used and operative time reported across both groups and propensity matched groups with p values.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Total energy, lasing time, intraop time reported (Table 2).
10. Was the exposure(s) assessed more than once over time?			✓	Reoperation during follow-up, however exact intervention not reported and timing of events not reported.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Complications by Clavien-Dindo grade (Table 2). IPSS, PVR, Qmax, PSA, and SUI reported.
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No mention of blinding
13. Was loss to follow-up after baseline 20% or less?			✓	Not reported
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	✓			Propensity matched, univariate and multivariate logistic regression analysis for predicting trifecta achievement (but only reported for propensity matched cohort).
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	Authors acknowledge limitations: retrospective analysis, high-volume centres (likely over learning curve), variability in follow-up protocols, mid-term follow-up, potential for unmeasured confounders to impact propensity matching (selection bias), sexual function not evaluated. Funding: no specific funding. The authors declare that they have no conflict of interest. Additional analysis on propensity matched cohort but not all cohort. Table 2 majority of results.			
Quality Rating	**Fair**			

Ghahhari *et al.* (2021)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"Aim of the study was to evaluate efficacy and efficiency of 180-watt Green-Light XPS laser photoselective vaporization of the prostate (PVP) in patients under 5-alpha-reductase inhibitors (5ARI) treatment."
2. Was the study population clearly specified and defined?	✓			"Patients with bothersome LUTS were offered surgery if preoperative IPSS ≥12 points and/or quality of life (QoL) ≥ 4 and/or maximal urinary flow rate (Qmax) <15 mL and/or not-responding to medical therapy and/or not willing to undergo medical therapy. "Any patient with a prior history of prostatic or urethral surgery, urethral stricture, neuro-vesical dysfunction and/or prostate cancer was excluded from the study."
3. Was the participation rate of eligible persons at least 50%?			✓CD	Number invited to participate not reported, "all patients undergoing GL-XPS PVP between February 2017 and September 2019 were prospectively enrolled. All patients signed informed consent", number of dropouts or participation rate not reported, no data flow diagram.
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	✓			Same inclusion and exclusion criteria applied to all. No trial registration.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification as to number of patients (likely pragmatic, all patients between Feb 2017 and Sept 2019). Study powered for some outcomes on post-hoc calculations; "Post-hoc power calculation confirmed a power >80% for all efficiency endpoints". P values reported for most outcomes although number of patients at each time point not reported.
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Cohort defined through use of GreenLight PVP. Subgroups defined by 5ARI use: "Patients were divided in two groups according to the chronic use (>6 months) of 5 ARI vs. no treatment." In statistical analysis section Group II included patients who had never taken 5ARI in the last 3 years."
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	✓			Although the timepoint for all outcomes not explicitly stated. IPSS, Qmax, PSA assessed at 3, 6 and 12 months, complications reported assessed at 3, 6 and 12 months, complications reported ≤30 days and >90 days, PGI-I outcome timepoint not reported.
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?		✓		Level of exposure to GreenLight PVP not applicable. However dose of 5ARI not reported (2 subgroups defined as >6 months use of 5ARI, or never used in past 3 years). Mixture of PVP and anatomical vaporisation.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and	✓			Lasing density, vaporisation efficiency, power recorded.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
implemented consistently across all study participants?				
10. Was the exposure(s) assessed more than once over time?		✓		Study reports re-intervention as a late complication but does not report what the additional interventions were.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?		✓		Unclear when PGI-I measured, unclear if median or mean hospital stay, catheterisation time. Table IV is for complications, however unclear how many patients these correspond to (total number of patients with early comp, late comp not explicitly reported). Statistical analysis on Table IV likely not significant due to number of subcategories and small numbers.
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No mention of blinding.
13. Was loss to follow-up after baseline 20% or less?			✓	Completeness of follow-up not reported.
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?		✓		No multi-variate analysis, many statistical comparisons with no correction applied.
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	Missing information through results; authors report no statistical significant difference in symptoms or QoL at baseline (referring to Table 1) however no rows associated with these outcomes. Post-hoc power calculation conducted for laser efficacy outcomes. Provides intraoperative details: energy usage (kJ), lasing time (min), operation time (min), lasing density (kJ/g), vaporisation efficiency (g/min), vaporisation power (kJ/min). Authors acknowledge limitations of single centre, lack of follow-up, lack of incontinence and overactive bladder questionnaires. The authors declare no conflict of interest.			

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
Quality Rating	Poor			

Ghahhari *et al.* (2018)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"We have analyzed our data with the aim of evaluating the efficacy- safety of the latest version of the GreenLight XPS™ laser system for standard PVP (532 nm-laser photovaporization with GreenLight XPS™) and the impact of this technique on perioperative and postoperative outcomes."
2. Was the study population clearly specified and defined?	✓			Patients undergoing PVP at single centre between February 2013 and April 2017. Single surgeon.
3. Was the participation rate of eligible persons at least 50%?			✓	Patient flow not reported. Number excluded due to missing preoperative characteristics not reported.
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?		✓		States that "Patients with missing preoperative characteristics were excluded from the analyses"; however these were not defined.
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification provided, likely pragmatic.
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Retrospective analysis, all patients underwent GreenLight and followed for outcomes. No trial registration reported.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?		✓		Median follow-up was 18 months (range 1-48 months). Change in IPSS, PSA, Qmax reported at 6 months. Post-operative complications recorded between hospital discharge and 6 months.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?		✓		Multiple PVP techniques used; "All patients underwent PVP, adopting the different techniques: standard PVP, anatomical PVP, and PEBE following the choice of the surgeon. All procedures were performed under general or spinal anesthesia and preoperative antibiotic prophylaxis was administered to all patients according local practice guidelines", outcomes not reported by procedure technique. Patient cohort included those on anticoagulant therapy and urinary retention but outcomes not reported exclusively.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Lasing time, operative time, energy use reported however not reported by procedure technique used (PEBE, standard, anatomical).
10. Was the exposure(s) assessed more than once over time?	✓			"Five patients underwent reoperation after first PVP."
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Complications reported via Clavien-Dindo classification. Change in IPSS, PSA, Qmax reported at 6 months.
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No blinding reported.
13. Was loss to follow-up after baseline 20% or less?			✓	Median follow-up 18 months (range 1-48 months). Number of patients with 6 month follow-up not reported.
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship		✓		No statistical comparisons (no p-values). Descriptive paper only.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
between exposure(s) and outcome(s)?				
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	One author reported tutoring honoraria from AMS, other authors had no conflicts to declare. No funding source reported. Authors acknowledge limitations of study, including: retrospective nature, non-randomised design, lack of subgroup analysis by prostate volume, surgeon learning curve for all three techniques, post operative outcomes based on clinical interview, sexual function not evaluated. . Results from standard PVP, anatomical PVP and PEBE all aggregated together (PEBE out of scope); only results in Table IV reported separately and relevant to assessment report.			
Quality Rating	**Poor**			

Goueli *et al.* (2017)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"We sought to determine the efficacy of 532 nm laser photovaporization with GreenLight 180 W XPS in men with preoperative urinary retention."
2. Was the study population clearly specified and defined?	✓			Retrospective study of patients treated with GreenLight PVP for BPH using XPS-180 W, performed at single tertiary centre, between 2011 and 2017.
3. Was the participation rate of eligible persons at least 50%?			✓	No patient flow diagram reported. Assuming all eligible were included but not explicitly reported (patient consent not described).
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	✓			Inclusion criteria defined. Reported 18 patients with known prostate cancer or prior radiation therapy, 36 patients treated with GreenLight HPS 120 W, and 38 with history of BPH surgery were excluded.
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification provided, likely pragmatic.
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Retrospective analysis of patient undergoing GreenLight PVP (applying different stratification to Pierce and Meskawi). No trial registration reported.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	✓			Median follow up of 24 months for IPSS, PVR, Qmax, QoL however does not explicitly report how many reached specified timepoints (3, 6, 12, 24 months. Complications reported as ≤30 days or >90 days.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?	✓			Lasing time, operative time, energy use, density, and number of irrigation bags reported by retention subgroups with p values.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Lasing time, operative time, energy used, number of irrigation bags, energy density.
10. Was the exposure(s) assessed more than once over time?			✓	Retreatment captured. However detail on the specific interventions and timing of interventions not reported.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Complications via Clavien-Dindo grade. Standard Qmax, IPSS and PVR functional outcomes. Assume QoL is IPSS-QoL.
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No mention of blinding.
13. Was loss to follow-up after baseline 20% or less?			✓	Median follow-up of 24 months, follow up reported at 3, 6, 12 and 24 months but the number of patients included at each time point not reported.
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?		✓		No multivariate analysis reported. No correct for multiple statistical comparisons. Paired statistics not reported for IPSS, Qmax, PVR or PSA comparisons at repeated follow-up intervals with baseline. However additional statistical analysis conducted to determine if any characteristics different between patients where PVP failed and those not. Patients with retention had greater prostate volume (median

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
				[IQR] 76 [57-105] ml versus 69 [45-79] ml, p<0.001), which will confound results.
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	Authors declare they have no conflict of interests. No funding reported. Authors acknowledge limitations of study: uncontrolled cohort design, two types of fibre used (majority with 180 W KTP laser fibre), multiple providers with variable experience, no measurements of bladder contractibility, did not record diabetes status or details regarding duration of diabetes. Study reports that "The majority of surgeries were performed as an outpatient procedure…" however this is unquantified. Potential overlap with Meskawi *et al.* (2017) and Pierce *et al.* (2021); although not confirmed.			
Quality Rating	**Fair**			

Knapp *et al.* (2017)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"The primary objective of the present study was to compare perioperative factors and AEs in men undergoing PVP with the 180-W LBO laser with or without continued anticoagulation therapy."
2. Was the study population clearly specified and defined?	✓			Patients undergoing PVP at single hospital between July 2010 and December 2016, retrospectively extracted from database. No exclusions listed.
3. Was the participation rate of eligible persons at least 50%?			✓	No patient flow diagram reported. Assuming all eligible were included but not explicitly reported (patient consent not described).
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?			✓	Assume inclusion criteria applied to all, however no exclusion criteria listed.
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification (assume pragmatic, number of procedures conducted within timeframe)
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Retrospective database review. No trial registration reported.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	✓			Study only considers complications therefore 90 day follow-up appears reasonable.
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the	✓			Lasing time, operation time, applied energy reported by antigoaculation therapy status.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?				
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Operation time, laser time, applied energy all recorded. Anticoagulation group included patients who continued use of heparin, warfarin, clopidogrel, dipyridamol and new oral anticoagulant (NOAC) medications; though dose not reported.
10. Was the exposure(s) assessed more than once over time?		✓		No repeated procedures (however reasonable given 90 day follow-up period as study is focusing on safety)
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Complications classified using Clavien-Dindo categories.
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No mention of blinding.
13. Was loss to follow-up after baseline 20% or less?			✓	Assume all patients followed to 90 days (although not explicitly stated).
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?		✓		No multi-variate analysis conducted, however multiple univariate tests reported (anticoag vs control, aspirin vs. control). No correction of multiple statistical tests.
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	One author declared participation on advisor board for Boston Scientific (manufacturer of GreenLight). Other authors declared no conflicts. No funding source reported. Authors acknowledge limitations of study including: retrospective nature, single surgeon, single centre series and therefore results may not be generalisable.			
Quality Rating	**Fair**			

Law *et al.* (2021)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"This descriptive analysis aims to characterize the current state of GL-PVP, pooling data from international centers." "we provide a descriptive analysis of preoperative, perioperative data, surgical complications, and functional outcomes"
2. Was the study population clearly specified and defined?	✓			Patients undergoing PVP by eight surgeons at seven international sites.
3. Was the participation rate of eligible persons at least 50%?			✓	From database (assume all eligible for data entry). No patient flow diagram reported.
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	✓			Similar populations (guideline variation by country). Inclusion and exclusion criteria stated. 24 patients with history of prostate cancer, 158 patients treated previously with TURP, 4 patients treated previously with pelvic radiation and 2 patients with neurological disorders were excluded.
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification provided (however pragmatic, likely all cases entered).
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Intrinsic to study design (database); cohort identified through use of GreenLight PVP. No trial registration reported.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	✓			Long follow-up (129 patients followed up to 60 months)
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the		✓		Vaporisation time, operative time, mean laser energy delivered, number of fibres used all reported over full

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?				cohort, no subgroup analysis or trends in data reported.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Vaporisation time, operative time, mean laser energy delivered, number of fibres used all reported.
10. Was the exposure(s) assessed more than once over time?			✓	Reintervention rates reported but specific procedure not noted; “within 60 months, BPH recurrence requiring surgical reintervention was seen in 10 (1.5%) patients”
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Standardised outcomes (IPSS, PVR, QoL, Qmax)
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No mention of blinding
13. Was loss to follow-up after baseline 20% or less?		✓		Measurements of PSA, IPSS, QoL, Qmax, PVR vary and drop off with time. Denominator clearly stated in all cases (Table 2). Followed up to 60 months, but median follow-up of 6 monhts.
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	✓			Correction for multiple statistical comparisons applied. Exploratory analysis using multivariable logistic regression modelling.
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	Conflict of interest: Consultants and proctors for Boston Scientific for Greenlight: KZ, DSE, VM, ER, and HC. Investigators and consultants for PROCEPT BioRobotics: VM, TB, NB, and KZ. Surgical tutors for Greenlight Xcelerated Performance System (American Medical System-AMS, Minnetonka, MN) and received honoraria for their tutorship: GF and LC. All the other authors do not report any relevant conflicts of interest. Funding: None			

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
	Authors acknowledge limitations: retrospective nature, long-term follow up is limited (return to primary care or community), lack of uniform follow-up, ejaculation/erectile function and subcategories of incontinence not reported.			
Quality Rating	**Good**			

Lee *et al.* (2016)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"In this study, we evaluated the safety and efficacy of PVP using 180 W XPS in patients from a large, international, and multi-institutional cohort on systemic anticoagulation."
2. Was the study population clearly specified and defined?	✓			Two centres (USA and Switzerland), from 2010 to 2013, patients undergoing 180 W GreenLight PVP for bladder outlet obstruction secondary to BPH according to American and European guidelines.
3. Was the participation rate of eligible persons at least 50%?			✓	No patient flow diagram reported. Assuming all eligible were included but not explicitly reported (patient consent not described).
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?			✓	Assume inclusion criteria applied to all, however no exclusion criteria listed.
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		Not justified (assume pragmatic, inclusion within dates; however not described as consecutive recruitment).
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Retrospective analysis. No trial registration reported.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	✓			IPSS, Qmax, PVR outcomes reported at 2 years.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?		✓		All patients treated with GreenLight. However subgrouped by medication (anticoagulation and not). However antiplatelets also included in anticoag arm (aspirin, clopidogrel and warfarin). “All men taking aspirin remained on therapy throughout the procedure and postoperatively. Clopidogrel was held 3 to 7 days before PVP, and was restarted on postoperative day 1. Of the men taking warfarin preoperatively, 35 (61.4%) remained on therapeutic levels of warfarin at the time of PVP with an international normalized ratio ≥ 2.” Operative time, lasing time, energy used and number of fibers reported by anticoagulation therapy status.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Operative time, lasing time, total energy, number of fibres recorded.
10. Was the exposure(s) assessed more than once over time?			✓	Reoperation rates reported across arms (detail on timing and type not reported).
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Assume QoL is the IPSS-QoL. Complications measured using Clavien-Dindo as stated in methods, but not reported per grade in results). IPSS, Qmax and PVR standard functional outcomes.
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No mention of blinding.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
13. Was loss to follow-up after baseline 20% or less?		✓		Numbers reported at 1 month: 247/384 (64%) and dropping to 2 years. However explicitly reported.
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?		✓		No multi-variate analysis performed. No correction for multiple statistical comparisons.
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	Authors acknowledge limitations of study including: retrospective nature, surgical experience variable across centres, tertiary centres may not be generalisable. Study defines large prostates as ≥60ml. Anticoagulation included use of antiplatelets: aspirin, clopidogrel, warfarin.			
Quality Rating	**Poor**			

Liu *et al.* (2020)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"In the present study, we evaluated the safety and efficacy of GreenLight XPS 180-W laser PVP in high-risk elderly patients with BPH."
2. Was the study population clearly specified and defined?	✓			All patients undergoing PVP between January 2016 and October 2018 in a single centre with a single surgeon.
3. Was the participation rate of eligible persons at least 50%?			✓	Assuming all eligible were included but not explicitly reported (patient consent not described).No data flow diagram reported.
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?			✓	Assume inclusion criteria applied to all however no exclusion criteria defined. Abstracts stated all patients were >80 years and had enlarged prostates (>40ml) but not listed in methods section. Patients considered high risk by definition due to cardiopulmonary disease, bleeding risk from oral anticoagylant use or excessive prostate volume (size not defined) were included. Patients recruited during same time period.
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification provided (likely pragmatic, all surgeries within timeframe).
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Retrospective analysis. All patients having GreenLight procedure and followed for outcomes. No trial registration reported.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	✓			Follow-up up to 12 months reported (average follow-up 13 months).

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?		✓		Operative time, laser time and energy used reported but not reported by patient subgroups (high risk). Patients with multi-morbid high risk factors not reported exclusively.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Operative time, laser working time, total energy reported (mean and range; Table 3).
10. Was the exposure(s) assessed more than once over time?	✓			PVP surgery successful, no conversion to open surgery or TURP. Before PVP, 16 patients underwent Holium laser lithotripsy for bladder stones, and 8 underwent implantation of a temporary pacemaker. Potential source of bias. Only one patient needed reoperation.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?		✓		Complications not reported using Clavien-Dindo classification. IPSS, QoL (assumed IPSS-QoL), Qmax and PVR, prostate volume and PSA reported 3, 6 and 12 months.
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No blinding reported.
13. Was loss to follow-up after baseline 20% or less?		✓		150 patients included, 147 at 3 months (98%), 139 at 5 months (93%), 94 at 12 months (63%).
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?		✓		No multivariate analysis, no statistical analysis reported (no p-values reported).
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	Authors reported no competing financial interests. Function was provided, in part, by the Natural			

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
	Science Foundation of Jiangsu Province, China and the Projects of Suzhou City, China.			
Quality Rating	**Poor**			

Meskawi *et al.* (2019)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"Based on these considerations, we examined the safety of PVP in patients on ATT. More specifically, we sought to focus on bleeding-related complications, stratified according to Clavien-Dindo grading system, and long-term efficacy and durability of GL PVP in patients on ATT at 2 years."
2. Was the study population clearly specified and defined?	✓			Retrospective study of patients treated with GreenLight 180 W PVP for BPH, "surgeries performed at a tertiary medical centre between 2011 and 2016 by an expert high-volume surgeon".
3. Was the participation rate of eligible persons at least 50%?			✓	No patient flow diagram provided. Assuming all eligible were included but not explicitly reported (patient consent not described).
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?			✓	Does not report "consecutive". Does not report that consent was required, does not mention ethics. Patients received intervention during the same time period.
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification but likely pragmatic
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Retrospective analysis of patient undergoing GreenLight PVP. No trial registration.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between	✓			Median follow up of 24 months (range 3-60 months). Complications recorded at 30

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
exposure and outcome if it existed?				and 90 days post PVP. IPSS, Qmax, QoL, PVR, and PSA reported at 3, 6, 12 and 24 months.
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?		✓		All patients had GreenLight PVP. Subgroups by medication. Dose, duration of use and combination not reported. Lasing time, operative time, energy used, number of fibers, and number of irrigation bags reported by subgroups
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Lasing time, operative time, energy used, number of fibres, energy density, irrigation bags.
10. Was the exposure(s) assessed more than once over time?			✓	Retreatment reported across all groups, however timepoint and detail of which intervention not reported.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Complications via Clavien-Dindo grade. Standard Qmax, IPSS and PVR functional outcomes. Complications reported intraoperatively, 30 days and 90 days.
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No mention of blinding.
13. Was loss to follow-up after baseline 20% or less?		✓		IPSS, Qmax, PVR and PSA reported at 3, 6, 12 and 24 months however it is not reported how many patients remained at each time point.
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	✓			Multivariate logistic regression analysis conducted to determine whether antithrombotic status was a predictor of serious bleeding events adjusting for age, prostate volume, retention status, comorbidity score, and 5Ari use). No

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
				correction for multiple statistical comparisons. Paired statistics not reported for IPSS, Qmax, PVR or PSA comparisons at repeated follow-up intervals with baseline. Prostate volume significantly different between subgroups (may confound results).
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	Neither funding nor conflicts of interest reported by the authors. Authors acknowledge limitations of study including: retrospective design, high volume surgeon. However the authors also note that a randomised trial with antithrombotics would be unfeasible due to the potential risk associated with gold standard TURP (unethical) Likley overlap with Meskawi *et al.* (2017)			
Quality Rating	**Fair**			

Meskawi *et al.* (2017)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"the purpose of this study was to examine the mid-term outcomes of Greenlight PVP in patients with a PV > 100 cc in a large multiinstitutional cohort. Particularly, durability and potential factors associated with higher retreatment rate were analyzed."
2. Was the study population clearly specified and defined?	✓			"We conducted a multiinstitutional, retrospective study of prospectively collected data for patients treated with Greenlight laser PVP for benign prostate hyperplasia (BPH) using the XPS-180 W system. Treatment indications were in accordance with the American, Canadian, and European clinical practice guidelines"
3. Was the participation rate of eligible persons at least 50%?			✓	Reported 10 patients with prostate cancer excluded. But number excluded due to missing data not reported. No patient flow diagram provided.
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?			✓	Retrospective extraction of data, all patients with prostate >100 ml included. Patients with missing pre-operative characteristics were excluded, however authors don't report which characteristics. Patients treated during same time period (2010 - 2015).
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification but likely pragmatic
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Retrospective analysis of patient undergoing GreenLight PVP. No trial registration reported.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	✓			Median follow up of 24 months (range 1-60 months); minimum 1 month due to patient death. IPSS, Qmax, PVR, and PSA reported at 6, 12, 24, 36 and 48 months. Retreatment rates reported at 12, 24 and 36 months. Complications were recorded between discharge and 6 months of PVP intervention.
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?			✓	Intraoperative variables reported as full cohort, number of patients with co-morbid variables (*e.g.* anticoagulant use, urinary retention) not reported or analysed exclusively.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Lasing time, operative time, energy used, number of fibres, energy density.
10. Was the exposure(s) assessed more than once over time?			✓	Retreatment captured at 12, 24, 36 and 48 months (timeframe captured). Detail on the specific interventions not reported, assumed to be PVP retreatment due to the reporting of energy delivered.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Complications via Clavien-Dindo grade. Standard Qmax, IPSS and PVR functional outcomes.
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No mention of blinding.
13. Was loss to follow-up after baseline 20% or less?		✓		Median follow-up of 24 months. IPSS at 6 months available in 345/438 (79%), and drops to 41/438 (9%) at 4 years.
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship		✓		No multivariate analysis reported. No correct for multiple statistical comparisons. Paired statistics not reported for IPSS,

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
between exposure(s) and outcome(s)?				Qmax, PVR or PSA comparisons at repeated follow-up intervals with baseline. However statistical analysis was included to determine which patients were at higher risk of reintervention.
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	Authors declare they have no conflict of interests. No funding reported. Authors acknowledge limitations of study: retrospective nature, heterogeneity between centres in terms of surgical technique and follow-up, Small patient numbers beyond 3 years.			
Quality Rating	Fair			

Rajih *et al.* (2017)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"In the current study, we evaluated the safety and short-term outcomes of GL-XPS for the treatment of symptomatic BPH in [high medical risk] HMR men classified by American Society of Anesthesiologists physical status score."
2. Was the study population clearly specified and defined?	✓			All patients diagnosed with LUTS secondary to BPH who underwent GreenLight XPS between August 2010 to August 2014 at five centres in USA and Canada. Indications for surgery based on AUA, CUA, and EAU guidelines. Exclusion criteria included prostate cancer, previous radiation therapy, neurological disease, and urethral stricture, or urinary incontinence prior to surgery. All perioperative data were retrospectively collected in a central database.
3. Was the participation rate of eligible persons at least 50%?	✓			"Data obtained for 956 patients of whom 941 had available ASA-PS scores." 273 high risk (ASA III, IV) and 668 low risk (ASA I, II)
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	✓			Eligibility criteria applied to all (database review). Differences in age, IPSS-QoL, prostate volume, current BPH medical therapy, anticoagulant use, antiplatelet therapy, urinary retention, location of surgery significantly different between subgroups). Patients underwent intervention during same time period.
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification but likely pragmatic.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Retrospective review of database (following patients undergoing GreenLight surgery). No trial registration reported.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?		✓		Limited to 6 months (poor reporting of follow-up). Focus on safety only (within 90 days, and between 90 days and 6 months assumed). Efficacy outcomes (IPSS, IPSS-QoL, Qmax, PVR, PSA) compared at 6 months.
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?	✓			Procedure time, laser time, energy used and density, number of fibres used reported in subgroups with p values. Not reported relating to anticoagulant use or previous retention. Subgroups as ASA I/II or III/IV.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Intraoperative details captured: procedure time, laser time, energy delivered, energy density, number of fibres.
10. Was the exposure(s) assessed more than once over time?			✓	Final table at end of paper (no heading, assumed to be Table 6) reports adverse events and surgical retreatment rates at 1, 3, 6 and 12 months however details of intervention not reported. Table and information not referenced in paper.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?		✓		Complications reported using Clavien-Dindo classification. Functional outcomes reported using standard IPSS, Qmax, PSA. However methods state: "Missing values of the continuous outcome measures were imputed by next observation carried backward." But unclear how many values missing.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No blinding reported.
13. Was loss to follow-up after baseline 20% or less?		✓		"Mean follow-up time in the HMR and control group, respectively, was 401±434 and 459±406 days, but data points were not collected past six months for the majority of subjects given high attrition. Long-term outcomes could not be assessed due to insufficient data past six months." Efficacy outcomes restricted to 6 months, however safety outcomes just state >90 days (unclear if cut of 6 months applied). No statistical comparison of follow-up duration.
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?		✓		No multivariate analysis. No correction for multiple statistical tests applied. Additional subgroup analysis of adverse events was performed to determine impact of anticoagulation.
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	"Supported by Boston Scientific Corporation". Five authors serve as consultants to Boston Scientific Corporation for GreenLight XPS. Authors acknowledge limitations of study including: use of ASA to stratify patient risk (Charlson comorbidity index could have been used), 5 centres could have introduce variability in results, retrospective nature, short follow-up. Authors express need for prospective randomised studies in high-risk groups.			
Quality Rating	**Poor**			

Reimann *et al.* (2018)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"The primary intention of this study was to evaluate the progression of GL-XPS in a high volume center for GLXPS (>350 patients in 4 years) with the primary outcome measurements of operation time (OT) and laser time (LT) with regard to prostate volume and year of surgery as specific parameters of experience."
2. Was the study population clearly specified and defined?	✓			Patients undergoing GreenLight PVP for symptomatic BPH between June 2010 and February 2015 at a single centre.
3. Was the participation rate of eligible persons at least 50%?			✓	No patient flow diagram provided. Assuming all eligible were included but not explicitly reported (patient consent not described).
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	✓			Outcomes reported per year (little statistical analysis reported).
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification provided but likely pragmatic.
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Retrospective design, all patients had GreenLight and outcomes followed thereafter. No trial registration reported.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?		✓		Median follow-up not reported (lack of systematic follow-up reported by authors in conclusions). Intraoperative complications summarised.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?	✓			Operative time and laser time considered against prostate volume and by year considered due to surgeon experience and increased device power.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Additional fibres, mean energy use and energy density reported across all years (no statistical comparison).
10. Was the exposure(s) assessed more than once over time?			✓	Reoperation rates referred to in methods but no data reported.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?		✓		Complications reported, but not aggregated by Clavien-Dindo classification. Other oucomes reported as standard,
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No blinding mentioned.
13. Was loss to follow-up after baseline 20% or less?			✓	Not explicitly reported.
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?		✓		No multivariate analysis reported. No correction for multiple statistical comparisons. Lack of statistical comparisons (Figure 1 legend).
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	One author reported receiving honoraria from Boston Scientific. No funding source reported. Authors acknowledge limitations of study, including: retrospective design, lack of systematic follow-up (no long-term outcomes), no direct evaluation on changes in surgical technique over time and influence on peri- and post-operative results.			
Quality Rating	**Poor**			

Tao *et al.* (2019)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"The purpose of our study was to evaluate the clinical efficacy and short-term outcome of novel 180 WXPS laser system in our units in China."
2. Was the study population clearly specified and defined?	✓			Patients undergoing GreenLight laser vaporisation of the prostate for LUTS secondary to BPH between April 2017 and April 2018. Surgical indications in line with Chinese Urological Association guidelines.
3. Was the participation rate of eligible persons at least 50%?			✓	No patient flow diagram provided. Assuming all eligible were included but not explicitly reported (patient consent not described).
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	✓			Inclusion criteria included Qmax <15 ml/s, and IPSS>7. Exclusion criteria: neurogenic bladder, diagnosis of prostate or bladder cancer, urethral stricture.
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification provided, likely pragmatic.
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Assume retrospective data collection. All patients underwent GreenLight and followed for outcomes. No trial registration.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	✓			Follow-up at 3, 6 and 12 months.
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the		✓		Operation time, laser time, energy applied reported across cohort with mean, SD and range however not reported relating to

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?				co-morbidities or prostate volume.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Operation time, laser time, energy applied reported.
10. Was the exposure(s) assessed more than once over time?			✓	"Only 2 cases required re-operation because of the enlargement of residual prostate." However duration and type of operation not explicitly reported.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Complications reported using Clavien-Dindo classification, IPSS, Qmax, PVR, change in prostate volume reported at 3, 6 and 12 months (n=102 at all time points).
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No blinding reported.
13. Was loss to follow-up after baseline 20% or less?	✓			Results state that all patients were followed up at 3, 6 and 12 months and no patients lost to follow-up.
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?		✓		No statistical analysis reported. Descriptive only.
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	Conflicts of interest and funding source not explicitly reported. Author acknowledge short follow-up as a limitation of the study. Include for reporting of rare adverse events.			
Quality Rating	**Poor**			

Thomas *et al.* (2019)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"We sought to assess the safety and efficacy of the 180 W XPS-GreenLight laser in patients with a BPH volume ≤40 mL."
2. Was the study population clearly specified and defined?	✓			"Only patients with small volume prostates size (<40 mL) were included. PVP were performed at a two-tertiary medical center between 2012 and 2016."
3. Was the participation rate of eligible persons at least 50%?			✓	No patient flow diagram provided. Assuming all eligible were included but not explicitly reported (patient consent not described).
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	✓			"Only patients with small volume prostates size (<40 mL) were included. PVP were performed at a two-tertiary medical center between 2012 and 2016. Patients with a history of prostate cancer, radiation therapy and chronic retention were excluded from the analysis. All treatment indications were in accordance with both American and Canadian clinical practice guidelines."
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification provided, likely pragmatic.
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Retrospective analysis of prospectively collected data. No trial registration.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	✓			Adverse events reported up to 30 days, IPSS, Qmax, PVR reported at 6 months. Median follow-up of 6 months, max. of 22 months (reported in discussion).

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?		✓		Lasing time, operative time, energy and fibres used with mean, median and IQR reported however no subgroup analysis performed or discussion relating to outcomes.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Lasing time, operative time, energy use, number of fibres, energy density reported.
10. Was the exposure(s) assessed more than once over time?			✓	Reoperation not reported.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Complications reported using Clavien-Dindo classification. PVR, Qmax, IPSS reported.
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No blinding reported.
13. Was loss to follow-up after baseline 20% or less?		✓		58 patients at baseline, 54 patients at 30 days (93%), 38 patients at 6 months (66%)
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?		✓		No multivariate analysis, no correction for multiple statistical tests.
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	Conflicts declared for several authors receiving funding from Boston Scientific. Funding source not reported. Authors acknowledge limitations of study, including: surgeons being experts, retrospective nature, small sample size, high attrition rate (due to follow-up in tertiary care – authors stating that in the US that follow-up likely to be in primary care). Use of anatomical vaporisation (only reported in discussion not methods).			
Quality Rating	**Poor**			

Trujillo *et al.* (2021)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"In this single center study, we evaluate and compare the efficacy, safety and functional outcomes of PVP with Greenlight™ Laser 180 W XPS between patients with prostates bigger and smaller than 80 mL."
2. Was the study population clearly specified and defined?	✓			All patients with LUTS secondary to BPE, who underwent GreenLight 180 W between 2012 and 2019 were included and their medical records reviewed. Only patients with insufficient data were excluded; however this is not explicitly defined.
3. Was the participation rate of eligible persons at least 50%?	✓			A total of 840 patients were analysed. However, Group 1: 381, Group 2: 206 (assume the remaining 253 patients had missing data).
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?			✓	Assumed though not explicitly stated. Patients underwent intervention during same time period.
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No power calculation, however all patients undergoing GreenLight included (as per first line in Methods section)
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Cohort defined by use of GreenLight. Retrospective design. No trial registration reported.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	✓			Median follow-up of 47 months, with maxim, up to 70 months.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?	✓			Surgery time, lasing time, and energy applied and density reported by subgroup with p values.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Surgery time, time of applied laser, energy applied, time of laser as a proportion of total surgery time, energy density all reported.
10. Was the exposure(s) assessed more than once over time?			✓	Reintervention for LUTS reported but no detail provided as to which interventions used, nor was the time to event reported.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?		✓		Complications reported using Clavien-Dindo, Improvement in IPSS reported (*e.g.* 103); however the EAC is unclear what this means given than max IPSS=35). Unclear which QoL score was used.
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No blinding reported
13. Was loss to follow-up after baseline 20% or less?			✓	Median and maximum follow-up reported, but the number followed to 1 year, 2 years etc not explicitly stated.
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?		✓		Subgroup analysis by prostate volume (<80ml, >80ml) but unclear how volume=80ml treated. No multi-variate analysis conducted. No correction for multiple statistical comparisons applied.
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	Conflicts and funding not reported. Authors acknowledge limitations of study: retrospective nature, loss to follow-up, various learning curve of surgeons. Authors conclude GreenLight PVP should be used as a first line alternative for treatment of larger prostate volumes (IQR, 89 to 115ml),			

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
	however stress that surgeon experience is important to avoid complications such as conversion and transfusion. Likely overlap with Barco-Costillo *et al.* (2020); although not explicitly confirmed.			
Quality Rating	**Poor**			

Trail *et al.* (2021)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"We aimed to evaluate the safety and feasibility of performing GL-PVP as a day-case procedure at our high-volume institution by comparing operative and functional outcomes in patients managed as a day-case with those who remained in hospital overnight postoperatively."
2. Was the study population clearly specified and defined?	✓			Consecutive patients who underwent GreenLight PVP at single centre between October 2016 and June 2016 inclusive.
3. Was the participation rate of eligible persons at least 50%?			✓	Exclusions not reported,no data flow diagram.
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	✓			*Consecutive* patients reported in outcomes. Interventions performed during same time period.
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No power calculation, consecutive patients reported within defined time frame (pragmatic)
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Retrospective review of electronic patient records. No trial registration reported.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	✓			Median follow-up of 27 months (400 patients had data available at 4 months, not reported how many had data available up to 27 months).
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the	✓			Operation time, laser energy and time reported across day-case and non-day-case subgroups with p values.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?				
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Laser energy delivery, operation time, laser time reported.
10. Was the exposure(s) assessed more than once over time?	✓			All subsequent operations reported, including revision GreenLight PVP.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Complications reported using Clavien-Dindo grade, Qmax, PVR standard function outcomes.
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No blinding mentioned.
13. Was loss to follow-up after baseline 20% or less?		✓		400/538 patients had data up to 4 months (74.3%), not reported how many had follow up at 1 year, 2 years, and so on.
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	✓			Univariate and multivariate analysis conducted.
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	Grant support: not applicable. Conflicts of interest not reported. Authors acknowledge limitations of study: retrospective nature, single centre, missing data in some patients, patient presentation to primary care will not be captured via retrospective electronic record review, patients followed up outside region would have gap in follow-up. Table headers in Table 4 confusing.			
Quality Rating	**Fair**			

Waters *et al.* (2021)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"Our study aimed to assess the utility and safety profile of GreenLight XPS PVP for treating BPH in high-risk patients."
2. Was the study population clearly specified and defined?	✓			Single surgeons experience of treating high-risk patients with GreenLight XPS PVP between two sites (Ireland) over a four-year period.
3. Was the participation rate of eligible persons at least 50%?			✓	No patient flow diagram provided. Assuming all eligible were included but not explicitly reported (patient consent not described).
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	✓			Patients were considered to be high risk if increased risk of bleeding, those with prostate size > 80ml (as per EAU guidelines 2015) or those with preoperative urinary retention. Age greater than 80 years, also considered to be high risk. Note that 20/103 patients aged over 80 years had previous TURP and 6/103 had previous PVP (Table 7).
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification provided,likely pragmatic.
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Retrospective study of prospective database. No trial registration reported.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?			✓	Readmissions captured, but length of follow-up not explicitly reported.
8. For exposures that can vary in amount or level, did the study			✓	Exposure outcomes not reported.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?				
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			✓	Operating duration, total energy, number of fibres not reported.
10. Was the exposure(s) assessed more than once over time?			✓	Delayed conversion to TURP reported, but repeated PVP not reported.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Complications defined using Clavien-Dindo classification.
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No mention of blinding.
13. Was loss to follow-up after baseline 20% or less?			✓	No reported duration of follow-up.
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?		✓		No statistical analysis reported (mainly descriptive).
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	Authors declare no conflict of interest, authors confirmed no financial support for the research, authorship or publication of the article. Authors acknowledge limitations of study, including: retrospective nature, single surgeon who performs a high volume of PVP cases (lack generalisablility).			
Quality Rating	**Poor**			

Xu *et al.* (2021)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"aims to evaluate the feasibility and safety of PVP in day-surgery pattern compared to the conventional inpatient pattern."
2. Was the study population clearly specified and defined?	✓			From April 2017 to March 2020 the clinical data of 312 patients with LUTS secondary to BPH who underwent 180 W XPS GreenLight was retrospectively analysed. All were classified as day-case or inpatient. Specifically excluded patients with prostate volume >100 ml. "Surgical indications were aligned with the BPH guideline of the Chinese Urological Association (CUA)".
3. Was the participation rate of eligible persons at least 50%?			✓	No patient flow diagram reported. Assuming all eligible were included but not explicitly reported (patient consent was required from all patients so participation may not be 100%).
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?			✓	Assume same inclusion criteria applied to all patients. However there are two sets of exclusion criteria, appears as though diifferent exclusions based on setting (day-case/inpatient).
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification provided, likelypragmatic.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Cohort defined by GreenLight surgery. Subgroups based on day-case or inpatient surgery. Assume given reporting of results that the subgroups were defined as the booked setting or intention (as some day-cases did stay overnight in hospital as an outcome).No trial registration.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	✓			1 year (mid-term outcomes), sufficient in terms of safety and patient outcomes. Longer term required for efficacy, however some cases of retreatment with TURP were identified.
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?	✓			Laser time, surgical time, energy density and consumption and number of fibres reported in subgroups (day-case, inpatient) with p values.
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Mean surgery time, laser time, energy consumption, energy density and number of fibres reported.
10. Was the exposure(s) assessed more than once over time?		✓		Reintervention with TURP reported.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Complications recorded using Clavien-Dindo categories, IPSS, Qmax, QoL (assumed to be IPSS-QoL), PVR standard outcomes.
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No mention of blinding.
13. Was loss to follow-up after baseline 20% or less?	✓			Follow-up explicitly reported (Table 4)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
				Day-cases (n=114): 107 at 3 months (94%), 95 at 6 months (83%), 77 at 12 months (68%) Inpatients (n=198): 191 at 3 months (96%), 176 at 6 months (89%), 135 at 12 months (68%).
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?		✓		No multivariate analysis. No correct for multiple statistical comparisons.
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	Authors declared no conflicts of interest. No funding source reported. Conclusions state: “In terms of patient selection, the systemic conditions of patients should be rigorously assessed by the urologist. For high-risk patients, such as patients with severe cardiopulmonary disease and cerebrovascular disease and those receiving long-term oral anticoagulant therapy, it is highly necessary to select them carefully for the day surgery. In addition, post-operative observation and health guides are equally important, especially for high-risk patients. Therefore, the medical staff should inform the patients of the potential complications and the corresponding emergency measures.”			
Quality Rating	**Poor**			

Zhou *et al.* (2017)
First reviewer (KK), Second reviewer (RP)

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
1. Was the research question or objective in this paper clearly stated?	✓			"This study aims at analyzing the impact of reaching current markers of proficiency on intra and postoperative clinical outcomes of laser vaporisation with 180 W GreenLight XPS in the treatment of benign prostatic hyperplasia." [However need to read methods to understand cohort is split into 8 groups of chronologically consecutive patients to analyse trends over time]
2. Was the study population clearly specified and defined?	✓			Patients undergoing GreenLight PVP using GreenLight 180 W XPS. High risk groups defined (but all risk groups included). Patients with diagnosis of prostate cancer were excluded.
3. Was the participation rate of eligible persons at least 50%?			✓	No data flow diagram. Eligibility not reported.
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	✓			Assume eligibility for GreenLight PVP remained the same (no change in guidance during study) although not explicitly reported. Consecutive patients recruited during set period, cohort retrospectively split into eight equal and consecutive groups of patients.
5. Was a sample size justification, power description, or variance and effect estimates provided?		✓		No justification provided, likely pragmatic.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	✓			Retrospective analysis. All patients having GreenLight procedure and followed for outcomes. No trial registration reported.
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	✓			Outcomes reported up to 1 year.
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (*e.g.*, categories of exposure, or exposure measured as continuous variable)?		✓		Peri-operative parameters including operating time, laser time, and energy used median and IQR with p values reported but not analysed by subgroups or patient risk although reported as significantly different over time (change of practice over time).
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Operating time, laser time, laser/operating time ratio, energy used, energy used/preoperative prostate volume reported
10. Was the exposure(s) assessed more than once over time?			✓	Retreatment reported (median 12 months (1-48 months) but type of retreatment not reported.
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓			Complications reported using Clavien-Dindo classification. Functional outcomes reported using PSA, Qmax, PVR, IPSS, IPSS-QoL.
12. Were the outcome assessors blinded to the exposure status of participants?			✓	No blinding reported.

Criteria	Yes	No	Other (CD, NR, NA*)	EAC Justification
13. Was loss to follow-up after baseline 20% or less?		✓		Cohort of 328 patients, 176 available at 6 months (53.7%), 152 at 12 months (46.3%), however some patients followed to 48 months (with those in the first subgroup of patients obviously having longer follow up than other subgroups).
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?		✓		Two approaches used to measure trend over time: 1) splitting into 8 groups (number not justified), 2) chronologically ranking by time. Bonferonni correction was applied for multiple comparisons. Proficiency determine as the number of interventions needed to reach a target level of ≥ 4 kJ/cm^3 (energy density) and a ≥50% PSA drop at 6 months – this definition is not referenced, source unknown. Large variability in Figure 1 – fit of logarithmic curve not reported. Stratification by prostate volume (≤80, >80 cm^3) to account for some confounding, but others not attempted (*e.g.* anticoagulant use).
*CD, cannot determine; NA, not applicable; NR, not reported				
Comment	Conflicts and funding not explicitly reported. Authors acknowledge limitations of the study, including: single centre, single surgeon (with previous experience of laser PVP therefore not reflective of complete learning curve), study lacks power for analysis of long-term outcomes.			
Quality Rating	**Poor**			

Appendix B4: Unpublished systematic review

The unpublished systematic review was critically appraised by the EAC using the PRISMA 2020 checklist (Page *et al.* 2021), Table B4.1. The aim of the unpublished systematic review was to identify relevant observational and comparative studies of laser therapies (not specific to GreenLight XPS) versus TURP in high-risk patients and determine any differences in safety and efficacy. The EAC notes that studies using 120 W and 180 W GreenLight devices were included and reported separately. The inclusion criteria reported a broader definition of high-risk when compared to that defined by the NICE Final Scope (NICE MT564 Final Scope, 2021) and included men:

- with a prostate larger than 80 ml,
- taking antithromotic agents,
- with urinary retention,
- aged over 80 years of age, or
- with significant comorbiditiy (not explicitly defined, assumed to be ASA grade 3 to 5 based on Results section).

The EAC notes that studies were excluded if “fewer than 50% of patients were high-risk and where the data is not reported exclusively”; therefore, the outcomes reported in the systematic review may not be exclusively those of a high-risk population. Due to the ambiguity in the inclusion and exclusion criteria set out in Table S4 and the lack of explicit reporting of studies contributing to each outcome, the EAC have been unable to verify the application of the inclusion and exclusion criteria for the included studies. The Company noted at fact-check that “authors did not include any studies with a mixed population unless there was a sub-group analysis for only the high-risk population”. The systematic review reports that for consistency, studies were categorised by the primary high-risk factor for which the patients were included in the study; however, it is unclear to the EAC how this was conducted in practice, as many studies have multiple inclusion criteria. For example, the study by Azizi *et al.* (2017) (which included 222 patients undergoing photoselective vaporisation of the prostate after propensity matching to 222 patients

undergoing vapour-incision technique; both arms using GreenLight 180 W) was categorised as large prostate in the systematic review. However, Table 4 of the study reports that only 185 of 444 patients (41.7%) had a prostate volume greater than 80 ml, and the breakdown of PVP or vapour-incision technique patients is not explicitly reported. The EAC acknowledges that 30.6% of patients had an ASA score of 3 or greater, and that 4.7% had reported anticoagulation use. However, as patient characteristics are not mutually exclusive, the EAC is unable to confirm whether this Azizi *et al.* (2017) meets the eligibility criteria of the systematic review (that is, the EAC is unable to confirm that the majority of patients, more than 50%, were considered high-risk).

The systematic review includes a clear data flow diagram (Figure S1) and reports that a total of 5,628 records were screened, 1,088 full text articles were assessed for eligibility, resulting in the inclusion of 157 papers reporting on relevant outcomes. The EAC notes inconsistencies and reasons for exclusion are not fully reported in Figure S1. For example, 1,088 full text articles were assessed for eligibility, following removal of 865 papers and reinclusion of 5 additional records identified through 'citation chasing', leaving 227 papers for review; however the EAC calculates that this should be 228 papers included for full review. The EAC assumes a miscalculation for excluded papers, as the reasons for exclusion add to 866 rather than 865. Additionally, Figure S1 reported 227 studies selected for full review (following removal of records excluded at full-text screening) with 157 included within the review; reasons for exclusion of the 70 papers are not explicitly reported (the flow diagram only states they reported a relevant outcome for a relevant intervention) or whether these are included within the excluded paper citations within Table S14.

A total of 28 studies (3,793 patients) using GreenLight 180 W were included in the systematic review (as determined from Table 1 of the unpublished manuscript); however, only 25 studies list GreenLight 180 W as the intervention in the supplementary Table S5; three are listed solely as 'GreenLight'. The EAC also notes that the intervention has not been correctly assigned in all papers. For example, the systematic review states that the intervention of Meskawi *et al.* (2019) was GreenLight 120 W in this study (Table S5); however the EAC notes that the intervention was clearly reported in the Methods section of the study as XPS-180W

(Boston Scientific) and that patients treated with HPS-120W system were explicitly excluded from analysis (Meskawi *et al.* 2019).

According to the systematic review Search Strategy and Study Selection, Medline, PubMed and Embase searches were conducted on 7 December 2020 (no limit applied to date of publication explicitly reported in search strategies, inclusion or exclusion criteria). The systematic review also included manual searches for relevant grey literature on 14 and 16 December 2020 (limited to 2 years prior; between 2018 and 2020). The EAC has crossed checked all studies with intervention states as GreenLight (regardless of stated power) from supplementary Table S5, against those included by the Company in the Clinical Submission, and those included by the EAC from their independent literature search, Table B4.2. A total of 15 studies identified by the EAC independent literature search included high-risk patients, but were not included in the unpublished systematic review, Table B4.3. The EAC note that 10 of these 15 studies were published after the systematic review search date (December 2020) including 2 studies conducted exclusively in high-risk patients (Waters *et al.* 2021; Mesnard *et al.* 2021), and 2 studies including more than 50% of patients considered high-risk (Gasmi *et al.* 2021; Trujillo *et al.* 2021). The EAC acknowledges that due to lack of detailed reporting of patient characteristics across studies that it may have been difficult to confirm whether the majority of patient cohorts were high-risk. However, highlights that all of the remaining five studies (all published before the search date of the systematic review) should have been identified by the systematic review literature search. The EAC would consider that two studies meet the eligibility criteria and were published before the search date and therefore should have been included in the systematic review (Hibon *et al.* 2017 was identified by the Company but excluded due to “no relevant data”, and Akhtar *et al.* 2018 was not identified).

The unpublished systematic review included eight conference abstracts with limited reporting of methods and results, and likely lack of peer-review (Ajitsaria *et al.* 2017; Andres *et al.* 2015; Chiu *et al.* 2019; Choudhary *et al.* 2016; Haudebert *et al.* 2020; Hueber *et al.* 2016; Mousa *et al.* 2018; Waters *et al.* 2018). The EAC excluded studies available in abstract form only from its literature search.

The systematic review states the total number of papers contributing to each outcome, but does not explicitly report *which* studies contributed. As the systematic review was not transparently reported, the EAC was unable to verify any of the values derived from the systematic review. In addition to this, authors report missing data for some of the included studies and it is not clear how these were handled. Some claims in the discussion are not supported by the results. For example, one principal finding of the systematic review state that in high-risk populations the benefits of treatment persist for at least 4 years with GreenLight. However, the authors also acknowledged the lack of studies with follow-up beyond 12 months. Therefore, it is unclear how robust the claim regarding longetivity of effect is. Additionally, the authors acknowledge that included studies were heterogeneous in terms of methodology, population, and outcomes reported. Another statement within the Conclusion section of the systematic report is that “many men with comorbidities are not offered surgery at all”; however the authors do not provide any evidence to suggest treatment is withheld. The Company also acknowledge the heterogeneity in their updated submission: “Burtt *et al.* (submitted) did not pool the means to conduct meta-analysis because of study heterogeneity”. Due to the heterogeneity preventing meta-analysis, the EAC questions the validity of applying the mid-point or upper value from outcomes reported in the systematic review within the updated economic model. Regarding conflicts of interests, the unpublished systematic review was funded by Boston Scientific (the manufacturer of the GreenLight device), with three out of eight authors being directly employed, two authors funded to conduct the research by Boston Scientific and the remaining three authors worked as consultants for Boston Scientific. The study acknowledges seven individuals who assisted in conducting abstract screening and data extraction with affiliations not stated.

As the systematic review missed eligible studies, included conference abstracts (lacking peer-review), was not explicit in the inclusion of only high-risk patients, was not transparently reported so that outcomes could be verified, included values where it is unclear how these have been derived, and acknowledged heterogeneity across included studies, the EAC would not consider its results robust enough to apply to economic modelling.

Table B4.1: PRISMA 2020 checklist, unpublished systematic review submitted by the Company

First reviewer: HAR; Second review: RP

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title: "Comparison of the Efficacy and Safety of Laser and Electrosurgical Transurethral Procedures for the treatment of BPO in high-risk patients: a systematic review." Page 5, Abstract, Methods: systematic literature review. Abstract, Results: 157 studies reviewed.
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Abstract follows appropriate format with Objectives, Methods, Results and Conclusions clearly structured. Authors define 'high-risk' differently compared to NICE document. NICE MT564 Final Scope, 2021 considers 'high-risk' patients as those with an increased risk of bleeding, have pacemakers or defibrillators, have prostates larger than 100 ml, or have urinary retention. The unpublished review defines 'high-risk' as patients with prostates larger than 80 ml, taking antithrombotic agents, with urinary retention, aged over 80 years, or have significant comorbidity (undefined).
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Introduction section provides a summary of clinical context and lack of evidence available for treatment in patients considered of 'high-risk'. Definition of 'high-risk' varies between the NICE final scope and the review; no justification for this is provided although authors note: Strengths and Limitations: "There is no universally-agreed definitions of 'high risk' so thresholds for reporting prostate size, in particular, varied across studies". Rationale lacks evidence to support the benefits of laser technologies seen in patients not considered of 'high-risk' may be applicable or appropriate to patients that are considered 'high-risk', although authors highlight a gap in knowledge of safety outcomes in this subgroup. There is no description or justification as to what the functional outcomes were or how these were measured.
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Final paragraph in Introduction section "this systematic literature review was conducted to identify relevant observational and comparative stuidies of GreenLight (120 and 180W), Holmium and Thulium laser therapies versus standard electrosurgical transurethral resection of the prostate (TURP) in high-risk patients and determine any differences in efficacy and safety". Specific measurements of

Section and Topic	Item #	Checklist item	Location where item is reported
			efficacy and safety not explicitly reported within the statement, although addressed in Introduction section.
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Materials and Methods: high-risk groups listed, although 'significant comorbidity' is not explicitly defined. Table S4: Inclusion and Exclusion Criteria: criteria for inclusion and exclusion were tabulated in PICOS format. The review identifies the report as being specific to 'high-risk' patients only, however the EAC note that the review included 'high-risk men' and excluded study cohorts where "less than 50% of the participants are 'high-risk' and where data is not reported exclusively". It is unclear whether this criteria included high-risk patient cohorts explicitly and whether cohorts with greater than 50% of patients considered high-risk were included. The inclusion of patients not considered of 'high-risk' contradicts the review objective to determine differences in efficacy and safety in 'high-risk' patients only. The EAC therefore consider the inclusion and exclusion criteria used to be inappropriate for the review objectives. Case studies with fewer than 5 participants were excluded, no justification was provided for this; the EAC note that case studies can be beneficial in providing inputs for rare adverse events.
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 3. Medline, Pubmed and Embase were searched for on 7th December 2020 with no date restrictions reported. Grey literature search was conducted on 14 December and 16 December (Table S3) with relevant literature from the 'past 2 years' from a range of sources. The EAC assumed this period was between 14 December 2018 and 16 December 2020 although not explicitly reported. The number of sources identified was defined, however specific references were not reported or how they contributed within the evidence review.
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplementary Tables 1-3, Figure S1 shows PRISMA diagram of literature flow although errors have been noted (see Point 16a). Reported limits applied are notes to be 'abstracts in humans'. No other limits have been explicitly reported.
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Search Strategy and Study Selection: "records were screened independently by two researchers according to the inclusion criteria in Table S4, and disagreements reconciled by discussion. All studies potentially meeting the inclusion criteria were retrieved and the full text screened for relevance. The citation lists of systematic reviews were searched to identify additional relevant publications."
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Search Strategy and Study Selection: "Data were extracted from the publications for all outcomes of interest by one researcher and checked by a second, with disagreements resolved by the project leader."

Section and Topic	Item #	Checklist item	Location where item is reported
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Types of Participants and Interventions Included: Efficacy and safety outcome measures defined although justifications for why these outcome measures were chosen or how they support efficacy and safety conclusions are not provided. Data for all available time points were given were recorded. Considerations for dealing with variables across a range of time points was not reported.
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Types of Participants and Interventions Included: Efficacy and safety outcome measures clearly defined. "Other details including baseline characteristics and funding were also extracted"; statement implies that additional details not described were collected. No detail of addressing missing or unclear information.
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Assessment of Risk of Bias: "Risk of bias was assessed by two researchers independenly using the Cochrane RoB2 tool for RCTs and questionnaires from the Joanna Briggs Institute for cohort and cross-sectional studies". Use of automation tools not reported.
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Assessment of Risk of Bias: "No formal statistical synthesis or sensitivity analyses of the results, assessment of publication bias or of the certainty of the body of evidence for each outcome was planned but data were summarised in tables and charts using R software functions". No further detail or justification of this provided.
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Table S5 provides a summary of the intervention characteristics against the high-risk population details. Details for the characteristics for relevant outcomes not reported and the studies contributing to each outcome not reported.
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Not stated, although authors note that no formal statistical synthesis was planned (Assessment of Risk of Bias section). Some inconsistencies and missing data points are also noted within Table 5, for example, some studies reported as GreenLight intervention without reference to power of device (120W or 180W) or how this was determined as in scope. Some follow-up time points were listed as unclear and it was not explicit how this was addressed within the review. In addition, the number of patients included within 3 studies (Grosso *et al.* 2020, Verrienti *et al.* 2019, Reimann *et al.* 2018) was reported as 'unclear' or 'NR' (assumed Not Reported, although no key given) despite a total number of patients included within the review is reported. Results: "157 studies had relevant data for the selected interventions and outcomes for this publication, from a total of 18,263 patients". Additionally, total number of patients included in high-risk subgroups of large prostates and other comorbidities was given, however included studies that did not report the number of participants. It is not clear how these were derived given the incomplete data sets.
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Assessment of Risk of Bias: "data were summarised in tables and charts using R software functions".

Section and Topic	Item #	Checklist item	Location where item is reported
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Not performed: Assessment of Risk of Bias: "No formal statistical synthesis or sensitivity analyses of the results, assessment of publication bias or of the certainty of the body of evidence for each outcome was planned but data were summarised in tables and charts using R software functions". No rationale or justification of this was provided. Authors note significant heterogeneity across the included literature although do not report how this was evaluated.
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Authors note significant heterogeneity across the included literature throughout the report, although do not report how this was evaluated nor are any methods to explore or address the heterogeneity described.
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Not performed: Assessment of Risk of Bias: "No formal statistical synthesis or sensitivity analyses of the results, assessment of publication bias or of the certainty of the body of evidence for each outcome was planned but data were summarised in tables and charts using R software functions". Strengths and Limitations: "Statistical comparisons were not feasible due to the heterogeneity in both study methodology and baseline characteristics". Authors note the inclusion of "studies where outcomes were reported for a group of patients with a prostate size of 80mL or more, or where the mean prostate volume and the lower margin of the 95% confidence interval for the study population were all above 80mL, but out subgroup of men at high risk due to prostate size is heterogeneous for this feature" (Strengths and Limitations). No further details provided regarding the robustness of the conclusions.
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Not explicitly stated, although a "risk of bias colour chart" was provided in Table S5, factors contributing to the evaluation is not reported. Handling of missing data generally not reported within the review, see point 13b.
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Not stated.
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Figure S1 shows PRISMA diagram of literature flow although stages are not clear and values are not consistent; 1,088 full test articles were assessed for eligibility, following removal of 865 papers and reinclusion of 5 additional records identified through 'citation chasing' this left 227 papers for review. The EAC assumes a miscalculation for excluded papers as the number of papers listed alongside exclusion reasons equals 866 rather than 865. The flow diagram also reports 227 studies were selected for full review and 157 studies reporting "relevant outcome for a relevant intervention" and included in publication, however it is unclear which papers these are and the reasons for why these were not excluded in the previous stage of full-text screening, or which studies these were or if they are included within Table S14.

Section and Topic	Item #	Checklist item	Location where item is reported
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Table S14 cites studies excluded at full text screening with reason. Reasons were classified as 'no relevant data', 'no high-risk group', 'systematic review', 'irretrievable', 'wrong intervention', 'duplicate publication'; however, Figure S1 PRISMA diagram reports 137 excluded due to 'irrelevant population'. The EAC are unable to verify the total and reason for study exclusion due to inconsistencies within the PRISMA diagram (Figure S1) and the number of papers included in Table S14.
Study characteristics	17	Cite each included study and present its characteristics.	Table S5, page 33; studies are reported with characteristics and single-arm studies are grouped by relevant high-risk subgroup, RCTs state relevant high-risk patient group within the chart. Narrative provided in Results section.
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Table S5, page 33, risk of bias colour chart provided, critical appraisal checklists not submitted to verify methodology. Results from risk of bias assessment reported as a colour chart in Table S5; no key was provided however the EAC assume a 'traffic light' system was used due to the use of red colour with '-' symbol, yellow colour with '?' symbol, green colour with '+' symbol. Additional information regarding risk of bias and cause of biases or uncertainties not explicitly reported.
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Findings, statistics or outcomes from each included study not reported, likely pragmatic due to the large quantify and variety of included literature. Ranges of outcomes were reported although the studies from which results were derived were not explicitly reported to enable verification.
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Each outcome summarised within the Results section. Summaries included brief summaries of results, however did not consistently compare interventions (purpose of review). Figures were taken from mean values across the literature, however no meta-analysis was performed and the studies included to derive figures were not explicitly reported to enable replication or verification. Risk of bias not reported for each outcome, unable to refer to risk of bias chart from Table S5 as studies included for each outcome not explicitly reported.
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Strengths and Limitations: "statistical comparisons were not feasible due to the heterogeneity in both study methodology and baseline characteristics". Meta-analyses not completed. Table S6 suggests pooled data, however it is not clear how these figures have been derived and there is poor reporting of which studies have been included (number of studies grouped by intervention; not all included studies report GreenLight power, and authors acknowledge inconsistent reporting of baseline characteristics).
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Authors acknowledge heterogeneity across the included literature; Strengths and Limitations: "statistical comparisons were not feasible due to the heterogeneity in both study methodology and baseline characteristics". Causes of heterogeneity not explicitly stated or explored. Authors note that "there is no universally-agreed definition of 'high-risk', so thresholds for reporting prostate size, in particular, varied

Section and Topic	Item #	Checklist item	Location where item is reported
			across studies', authors do not explicitly explore other reasons for heterogeneity, nor identify their justification for the definitions used within the systematic review.
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Sensitivity analyses not conducted.
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Not reported, authors report risk of bias was assessed with the RoB2 tool with results reported in colour chart in Table S5. Authors note that there statistical comparisons were not possible due to heterogeneity in baseline characteristics but do not explicitly report whether any results were missing or any reporting biases were assessed.
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Mean and median reported for some outcomes only. Confidence intervals or certainty of the body of evidence not reported.
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Discussion: "These fears and the lack of comparative evidence also mean that many high-risk men are not offered surgical intervention for BPO", the EAC consider this statement to be unjustified given the volume of evidence included within the literature review including patients considered of high-risk. Authors acknowledge variations in definition of 'high-risk' and provide no evidence supporting treatment being withheld from patients considered of high-risk. Authors report that the review "provides important new knowledge to guide the management of these hard-to-treat patients" based on summarising observational evidence in the treatment of 'high-risk' patients; this statement is not supported as the summary does not provide new knowledge, rather summarises existing knowledge. Authors acknowledge heterogeneity, however do not acknowledge that the findings include studies where only 50% or more of the included participants are considered 'high-risk' and provide rationale for why conclusions are robust and exclusive to patients considered of 'high-risk'. Only 3 papers were cited in the discussion - all previously published systematic reviews. The arguments made in paragraphs 1-5 were done with little context of other evidence.
	23b	Discuss any limitations of the evidence included in the review.	Authors acknowledge heterogeneity, lack of clearly defined 'high-risk' characteristics, variation in follow-up timepoints, and inconsistent reporting of outcomes. Authors do not acknowledge that the findings include studies where only 50% or more of the included participants are considered 'high-risk' and how conclusions are robust when considered exclusively in 'high-risk' patients.
	23c	Discuss any limitations of the review processes used.	Limitations relate to the "generally incomplete and inconsistent reporting of data from observational discussion" limiting statistical analyses due to heterogeneity; authors

Section and Topic	Item #	Checklist item	Location where item is reported
			do not identify how heterogeneity was assessed or addressed and no discussion regarding limitations of the review processes used by the authors.
	23d	Discuss implications of the results for practice, policy, and future research.	Discussion: "Future research should aim to report outcomes and complications in a more standardised way so the relative benefits and harms of these and new interventions can be better determined". Authors acknowledge ethical considerations of conducting RCTs in high-risk populations. Conclusion: Authors summarise "In high-risk patients the data available generally support the conclusion that laser therapies are able to provide comparable functional outcomes to electrosurgery and have overall safety benefit, with specific benefits in high-risk subgroups". Specific benefits not explicitly reported and studies summarised include patients not considered of 'high-risk' and so it is unclear how these benefits were determined. Authors state that benefits of GreenLight "persist for at least 4 years", however also acknowledge a lack of studies with follow-up beyond 12 months. Authors also state: "Many men with comorbidities are not offered surgery at all, which seems unreasonable in the age of laser prostatectomy", no evidence has been provided by authors demonstrating the withholding of treatment of patients considered of 'high-risk', rather 157 studies including 'high-risk' patients have been included within the review. Authors have demonstrated that all interventions are feasible in 'high-risk' patients and so this statement is leading and not supported by the evidence summarised within the literature review.
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Not reported. The EAC searched the PROSPERO database on 04/04/2022 with no results identified relating to the systematic review.
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Not reported.
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not reported.
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Funding: "This research was funded by Boston Scientific" (manufacturer of one of the interventions), role of funders not explicitly reported, however 3 authors are employed by Boston Scientific, two authors (employed by another Company) received funding to conduct the research and the remaining three authors have worked as consultants for Boston Scientific. High risk of bias.
Competing interests	26	Declare any competing interests of review authors.	Declaration of Interest/Competing Interests: 3 authors are employed by Boston Scientific (manufacturer of one of the interventions), 2 authors (employed by another Company) received funding to conduct the research and the remaining 3 authors have worked as consultants for Boston Scientific. Acknowledgements list 7

Section and Topic	Item #	Checklist item	Location where item is reported
			individuals who assisted in “conducting the abstract screening and data extraction for this literature review”, affiliations not stated. High risk of bias.
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Not reported.

Table B4.2: Summary of studies included in the unpublished systematic review, compared to the studies included in the Company clinical submission, and studies included by the EAC in the clinical submission.

		Unpublished systematic review	Company clinical submission	EAC		
#	STUDY (author, year)	Included	Included	Included	Excluded	Reason(s) for exclusion
1.	Abolazm *et al.* 2020		✓	✓		
2.	Aboutaleb *et al.* 2018			✓		
3.	Ajitsaria *et al.* 2017	✓			✓	Intervention: GreenLight 120W Study design: available as conference abstract only [Note high-risk not defined]
4.	Akhtar and Raina 2018		✓	✓		
5.	Altay *et al.* 2014	✓			✓	Date: before 2015 (MTG29 published)
6.	Andres *et al.* 2015	✓			✓	Language: only abstract available in English Intervention: does not appear to use GreenLight (Ceralas® HPD180W stated in methods)
7.	Azizi *et al.* 2017	✓		✓		
8.	Bach *et al.* 2017	✓			✓	Intervention: power not explicitly reported
9.	Bachmann *et al.* 2012	✓			✓	Date: before 2015 (MTG29 published)
10.	Bajic *et al.* 2019		✓		✓	Intervention (Device power setting: 80 W vaporisation, 35 W coagulation, GreenLEP)
11.	Barco-Castillo *et al.* 2020	✓	✓	✓		
12.	Berquet *et al.* 2015			✓		
13.	Brant *et al.* 2020		✓		✓	Intervention (Power setting not reported)
14.	Cacciamani *et al.* 2019		✓		✓	Study design (Systematic review, N=5 comparing GreenLight to TURP: *Bachmann et al. 2013 (80 W);* *Capitan et al. 2011 (120 W);* *Horasanli et al. 2008 (80 W);* *Lukacs et al. 2012 (120 W);* *Xue et al. 2012 (120 W)*
15.	Cakiroglu *et al.* 2013	✓			✓	Intervention: GreenLight 120W Date: before 2015 (MTG29 published)
16.	Campobasso *et al.* 2020	✓	✓	✓		

		Unpublished systematic review	Company clinical submission	EAC		
#	STUDY (author, year)	Included	Included	Included	Excluded	Reason(s) for exclusion
17.	Castellani *et al.* 2021		✓		✓	Study design (systematic review, N=14 comparing GreenLight to TURP: *Al-Ansari et al. 2010 (120 W);* *Kumar et al. 2016 (120 W);* *Purkait et al. 2017 (80 W);* *Ruskat et al. 2008 & Guo et al. 2015 (80 W);* *Tasci et al. 2008 (80 W);* *Telli et al. 2015 (120 W);* *Tugcu et al. 2008 (80 W);* *Bachmann et al. 2013 & Thomas et al. 2016 (80 W);* *Mordasini et al. 2018 (80 W);* *Pereira-Correia et al. 2011 (120 W);* *Xue et al. 2013 (120 W);* *Reimann et al. 2019 (180 W))*
18.	Castellucci *et al.* 2020		✓	✓		
19.	Chen *et al.* 2013a	✓			✓	Intervention: GreenLight 120W Date: before 2015 (MTG29 published)
20.	Chen *et al.* 2013b	✓			✓	Intervention: GreenLight 120W Date: before 2015 (MTG29 published)
21.	Chen and Chiang 2016			✓		
22.	Chiu *et al.* 2019	✓			✓	Study design: available as conference abstract only
23.	Choudhary *et al.* 2016	✓			✓	Intervention: GreenLight 120W Study design: available as conference abstract only
24.	Cimino *et al.* 2017			✓		
25.	Cindolo *et al.* 2017			✓		
26.	Contreras *et al.* 2021		✓	✓		
27.	Culkin *et al.* 2014		✓		✓	Intervention (not GreenLight)
28.	Destefanis *et al.* 2021		✓	✓		
29.	Eken and Soyupak 2018	✓		✓		
30.	Eken *et al.* 2017	✓			✓	Intervention: GreenLight 120W

		Unpublished systematic review	Company clinical submission	EAC		
#	STUDY (author, year)	Included	Included	Included	Excluded	Reason(s) for exclusion
31.	Elshal *et al.* 2020		✓		✓	Intervention: GreenLight laser vapo-enucleation
32.	Fang *et al.* 2015	✓			✓	Language: available in Chinese only Intervention: GreenLight 120W (apparent from title)
33.	Ferrari *et al.* 2021		✓		✓	Intervention (en-bloc GreenLEP, Device power: 120 W vaporisation, 20 W coagulation)
34.	Frendl *et al.* 2021		✓		✓	Intervention (photoselective vaporisation without specific reference to GreenLight, Device power not reported)
35.	Gasmi *et al.* 2021		✓	✓		
36.	Ghahhari *et al.* 2018		✓	✓		
37.	Ghahhari *et al.* 2021		✓	✓		
38.	Gilfrich *et al.* 2021		✓		✓	Intervention (photoselective vaporisation without specific reference to GreenLight, Device power not reported)
39.	Gomez-Sancha *et al.* 2015		✓		✓	Study design (narrative on enucleation procedure)
40.	Gondran-Tellier *et al.* 2021	✓	✓	✓		
41.	Goueli *et al.* 2017	✓	✓	✓		
42.	Gravas *et al.* 2021		✓		✓	Study design (EAU guidelines for LUTS and BPO)
43.	Gu *et al.* 2020		✓		✓	Study design (systematic review: comparison of GreenLight versus bipolar TURP: *Peng et al. 2016 (80 W);* *Kumar et al. 2013 (120 W);* *Kumar et al. 2018 (120 W);* *Liu et al. 2014 (full text not available in English);* Chimino *et al.* 2017 (180 W); comparison of GreenLight versus bipolar enucleation: *Wang et al. 2017 (full text not available in English);* *Mu et al. 2017 (100-160 W)*
44.	Gu *et al.* 2012	✓			✓	Date: before 2015 (MTG29 published)

		Unpublished systematic review	Company clinical submission	EAC		
#	STUDY (author, year)	Included	Included	Included	Excluded	Reason(s) for exclusion
45.	Haudebert *et al.* 2020	✓			✓	Study design: available as conference abstract only
46.	Hibon *et al.* 2017		✓	✓		
47.	Hueber *et al.* 2012	✓			✓	Intervention: GreenLight 120W Date: before 2015 (MTG29 published)
48.	Hueber *et al.* 2016	✓			✓	Study design: available as conference abstract only
49.	Hueber *et al.* 2015	✓			✓	Date: 2015 (included in MTG29)
50.	Huet *et al.* 2019	✓			✓	Outcomes: Treated as single-arm study (comparator out of scope), rare adverse events not reported, not tabulated by EAC
51.	Jaeger *et al.* 2015	✓			✓	Intervention: GreenLight 120W/180W (not reported exclusively)
52.	Knoblauch *et al.* 2019		✓		✓	Language (full text not available in English)
53.	Kiba *et al.* 2020		✓		✓	Intervention (power setting 120 W)
54.	Kini *et al.* 2020		✓		✓	Intervention (power setting not defined)
55.	Knapp *et al.* 2017	✓		✓		
56.	Kobayashi *et al.* 2021		✓		✓	Intervention (power setting 120 W)
57.	Laine-Caroff *et al.* 2021		✓		✓	Intervention (mixed power setting, 120 W used until 2011)
58.	Lanchon *et al.* 2018	✓	✓		✓	Comparator (open prostatectomy)
59.	LaRussa *et al.* 2021		✓		✓	Study design (systematic review, N=13: *Bachmann et al. 2005 (power not specified);* *Bouchier-Hayes et al. 2010 (80 W);* *Bowen et al. 2013 (120 W);* *Capitan et al. 2011 (120 W);* *Horasanli et al. 2008 (80 W);* *Mithani et al. 2018 (Intervention: Biolitec laser);* *Mohanty et al. 2012 (80 W);* *Nomura et al. 2009 (80 W);* *Pereira-Correia et al. 2012 (120 W);* *Purkait et al. 2017 (80 W);* *Tasci et al. 2008 (power not specified);*

		Unpublished systematic review	Company clinical submission	EAC		
#	STUDY (author, year)	Included	Included	Included	Excluded	Reason(s) for exclusion
						Thomas et al. 2016 (180 W), Tugcu et al. 2008 (power not specified))
60.	Law *et al.* 2021		✓	✓		
61.	Lee *et al.* 2016	✓		✓		
62.	Lee *et al.* 2014	✓			✓	Date: before 2015 (MTG29 published)
63.	Leonardo *et al.* 2020		✓		✓	Study design (systematic review, N=1 using GreenLight: *Skolarikos et al. 2008 (80 W, comparator open prostatectomy))*
64.	Liu *et al.* 2020	✓	✓	✓		
65.	Mathieu *et al.* 2017			✓		
66.	Mattevi *et al.* 2020		✓	✓		
67.	Meskawi *et al.* 2017	✓	✓	✓		
68.	Meskawi *et al.* 2019	✓	✓	✓		
69.	Mesnard *et al.* 2021			✓		
70.	Misrai *et al.* 2015	✓	✓		✓	GreenLEP Study design (video and abstract)
71.	Misrai *et al.* 2016	✓	✓		✓	Intervention (GreenLight PVP 120-180 W compared with GreenLEP 120 W)
72.	Moiroud *et al.* 2019	✓			✓	Outcomes: Treated as single-arm study (comparator out of scope), rare adverse events not reported, not tabulated by EAC
73.	Mousa *et al.* 2018	✓			✓	Study design: available as abstract only
74.	Mustafa *et al.* 2019	✓			✓	Intervention: GreenLight 120W
75.	Nicholson *et al.* 2015	✓			✓	Date: 2015 (included in MTG29)
76.	Nguyen *et al.* 2020		✓		✓	Study design (data pooled from 5 sources. GreenLight PVP from single study: Azizi *et al.* 2017 (180 W))
77.	Nguyen *et al.* 2021		✓		✓	Study design: subset of Law *et al.* 2021 (included)
78.	Ow *et al.* 2018	✓			✓	Intervention: GreenLight 120W
79.	Panthier *et al.* 2020		✓		✓	Intervention (GreenLEP, 120 W)
80.	Pathak *et al.* 2017	✓			✓	Intervention: GreenLight power not explicitly reported

		Unpublished systematic review	Company clinical submission	EAC		
#	STUDY (author, year)	Included	Included	Included	Excluded	Reason(s) for exclusion
81.	Peng *et al.* 2020		✓		✓	Study design (meta-analysis, N=6; *Elmansy et al. 2010 (NR);* *Elmansy et al. 2012 (120 W);* *Elshal et al. 2014 (60-120 W);* *Jaeger et al. 2015 (120/180 W);* *Kim et al. 2016 (120 W);* *Sun et al. 2019 (120 W))*
82.	Pierce *et al.* 2021		✓	✓		
83.	Piotrowicz *et al.* 2018	✓			✓	Intervention: GreenLight 120W
84.	Plata *et al.* 2021		✓		✓	Outcomes: Treated as single-arm study (comparator out of scope), rare adverse events not reported, not tabulated by EAC
85.	Prudhomme *et al.* 2020		✓		✓	Intervention (power setting, HPS fibres 120 W)
86.	Rajih *et al.* 2017			✓		
87.	Rapisarda *et al.* 2019		✓		✓	Study design (review, N=1, NICE guidance)
88.	Reale *et al.* 2020		✓	✓		
89.	Reimann *et al.* 2018	✓		✓		
90.	Reimann *et al.* 2019			✓		
91.	Ruszat *et al.* 2008	✓			✓	Intervention: GreenLight 80W Date: before 2015 (MTG29 published)
92.	Sachs *et al.* 2020		✓		✓	Intervention (power setting: NR)
93.	Salciccia *et al.* 2021		✓		✓	Study design (systematic review, N=5; *Osterberg et al. 2013 (120 W);* *Ben-Zvi et al. 2013 (120 W vs 180 W, including in original MTG29);* *Bowen et al. 2013 (120 W);* *Berquet et al. 2015 (180 W);* *Corbel et al. 2014 (180 W, full text not available in English))*
94.	Schwarz *et al.* 2021		✓		✓	Study design (review)
95.	Soans *et al.* 2020		✓		✓	Study design (systematic review, N=2; *Terrasa et al. 2013 (120 W);* *Elshal et al. 2012 (NR))*

		Unpublished systematic review	Company clinical submission	EAC		
#	STUDY (author, year)	Included	Included	Included	Excluded	Reason(s) for exclusion
96.	Sohn *et al.* 2011	✓			✓	Intervention: GreenLight 120W Date: before 2015 (MTG29 published)
97.	Stone *et al.* 2016		✓		✓	Intervention (power setting: NR)
98.	Sun *et al.* 2019		✓		✓	Intervention (power setting: 120 W)
99.	Sun *et al.* 2018	✓			✓	Outcomes: Treated as single-arm study (comparator out of scope), rare adverse events not reported, not tabulated by EAC
100.	Tao *et al.* 2013	✓			✓	Intervention: GreenLight 120W Date: before 2015 (MTG29 published)
101.	Tao *et al.* 2019			✓		
102.	Thomas *et al.* 2019			✓		
103.	Thoulouzan *et al.* 2017		✓		✓	Language (full text not available in English)
104.	Trail *et al.* 2021		✓	✓		
105.	Trujillo *et al.* 2021		✓	✓		
106.	Valdivieso *et al.* 2018	✓	✓	✓		
107.	Vanalderwerelt *et al.* 2021		✓		✓	Intervention (mixed device and power setting: KTP 80 W, HPS 120 W, XPS 180 W)
108.	Vasudeva *et al.* 2019	✓			✓	Intervention: 120W
109.	Waters *et al.* 2018	✓			✓	Intervention: GreenLight power not explicitly reported Study design: available as conference abstract only
110.	Waters *et al.* 2021			✓		
111.	Woo *et al.* 2011a	✓			✓	Intervention: GreenLight 120W Date: before 2015 (MTG29 published)
112.	Woo *et al.* 2011b	✓			✓	Intervention: GreenLight 120W Date: before 2015 (MTG29 published)
113.	Xu *et al.* 2021		✓	✓		
114.	Yoo *et al.* 2017		✓		✓	Intervention (power setting: 120 W)
115.	Yu *et al.* 2021		✓		✓	Intervention (power setting: 80 W)
116.	Zang *et al.* 2012	✓			✓	Language: available in Chinese only Intervention: GreenLight 80W and 120W Date: before 2015 (MTG29 published)

		Unpublished systematic review	Company clinical submission	EAC		
#	STUDY (author, year)	Included	Included	Included	Excluded	Reason(s) for exclusion
117.	Zheng *et al.* 2019		✓		✓	Study design (N=11; *Ruszat et al. 2007 (80 W);* *Woo et al. 2008 (120 W);* *Karatas et al. 2010 (80 W);* *Chen et al. 2013 (120 W);* *Choi et al. 2013 (120 W);* *Shao et al. 2013 (120 W);* *Sohn et al. 2013 (120 W);* *Chen et al. 2013 (120 W);* *Lee et al. 2016 (180 W);* *Knapp et al. 2017 (180 W);* *Piotrowicz et al. 2018 (120 W))*
118.	Zhou *et al.* 2017			✓		
119.	Zhou *et al.* 2021		✓		✓	Study design (meta-analysis, N=4; *Kobayashi et al. 2020 (120 W);* *Guo et al. 2015 (120 W);* *Chiang et al. 2010 (120 W);* *Ruszat et al. 2009 (120 W))*
	Total	**52**	**65**	**27**	**38**	

Table B4.3: Summary of studies which included high-risk patients not included in the unpublished systematic review

#	Study	Study design (n)	High-risk characteristics	EAC comment	Identified by unpublished systematic review
1.	Waters *et al.* 2021	Retrospective cohort (374)	Patients at high-risk of bleeding, those with prostate volume greater than 80ml, pre-operative urinary retention or aged greater than 80 years (where all patients had at least one high-risk factor)	Exclusively high-risk	Published after the systematic review search dates
2.	Mesnard *et al.* 2021	Retrospective cohort (5 TURP, 5 GreenLgith, 3 simple prostatectomy)	Patients with haemophilia	Exclusively high-risk	Published after the systematic review search dates
3.	Akhtar *et al.* 2018	Prospective cohort (34)	ASA class III and IV: 54% Catheterised on admission: 24% Age, years (range): 68.7 (53 to 87) Prostate volume, ml (range): 57.1 (10 to 162) Antiplatelet medication: 41%	>50% high-risk **Should have been incorporated in systematic review**	Not identified
4.	Destefanis *et al.* 2021	Retrospective cohort (76)	Anticoagulation therapy: 36.8% Indwelling catheter: 23.7% ASA score 3: 42.1% Prostate volume, cc (IQR): 63.5 (54.5 to 98.5)	Unable to confirm whether majority were high-risk	Published after the systematic review search dates
5.	Gasmi *et al.* 2021	Prospective cohort (1,491)	ASA score 3 or 4: 28.1% Anticoagulant/antiplatelet treatments: 54.2% Indwelling catheter: 66.5%	>50% high-risk	Published after the systematic review search dates
6.	Ghahhari *et al.* 2018	Retrospective cohort (140)	ASA score 3 or 4: 14.2% Aspirin use: 22% Antiplatelet use: 8.5% Anticoagulant use: 2.8% Indwelling catheter: 15% Prostate volume, median IQR: 60 (49 to 90)	Unable to confirm whether majority were high-risk	Yes (reason for exclusion: “No high-risk group”)
7.	Ghahhari *et al.* 2021	Prospective cohort (193)	Prostate volume, median IQR: 60 (50 to 84) ml Urine retention: 14%	Unable to confirm whether majority were high-risk	Published after the systematic

			Antiplatelet: 27% Anticoagluant: 6.2%		review search dates
8.	Hibon *et al.* 2017	Prospective non-randomised (106)	PVP Age, mean (SD): 71.5 (9.8) years ASA score, 3 or 4: 24% Prostate volume, mean (SD): 83.0 (33.8) ml Foley catheterisation: 24% Acetylsalicylic acid: 35% Clopidogrel: 7% Anti-vitamin K: 9% Rivaroxaban: 0% Anatomical vaporisation Age, mean (SD): 69.6 (9.1) years ASA score, 3 or 4: 20% Prostate volume, mean (SD): 93.5 (38.2) ml Foley catheterisation: 31% Acetylsalicylic acid: 25% Clopidogrel: 4% Anti-vitamin K: 10% Rivaroxaban: 2%	>50% high-risk (based on mean prostate volume) **Should have been incorporated in systematic review**	Yes (reason for exclusion: "No relevant data")
9.	Law *et al.* 2021	Retrospective cohort (3,627)	Prostate volume, median (IQR): 64 (47 to 90) cc Antithrombic therapy (other than aspirin): 34.3% ASA score of 3 of higher: 28.5%	Unable to confirm whether majority were high-risk	Published after the systematic review search dates
10	Mattevi *et al.* 2020	Prospective non-randomised (50 GreenLight, 50 TURP)	PVP Anticoagulants/antiplatelet: 38% ASA score 3: 34% TURP Anticoagulants/antiplatelet: 36% ASA score 3: 22%	Unable to confirm whether majority were high-risk	Not identified
11	Pierce *et al.* 2021	Retrospective cohort (424)	Normal weight Prostate volume, mean (SD): 67.9 (33.2) cc Hypertension: 46% Anticoagulant use: 24%	Unable to confirm whether majority were high-risk	Published after the systematic review search dates

			Overweight Prostate volume, mean (SD): 81.3 (43.2) cc Hypertension: 55% Anticoagulant use: 25% Obese Prostate volume, mean (SD): 73.7 (33.3) cc Hypertension: 69% Anticoagulant use: 27%		
12	Plata *et al.* 2021	Retrospective cohort (271: 158 normal contractility, 113 detrusor underactivity)	Normal contractility Anticoagulation: 2.5% History of acute urinary retention: 21.8% Prostate volume, median (IQR): 65 (45.5 to 95) ml Detrusor underactivity Anticoagulation: 7.1% History of acute urinary retention: 26.5% Prostate volume, median (IQR): 60.5 (41.4 to 80) ml	Unable to confirm whether majority were high-risk	Published after the systematic review search dates
13	Reale *et al.* 2020	Retrospective cohort (1,077)	Anticoagulant/antiplatelet therapy: 43.6% Urethral stricture (penile urethra): 4.3% Urethral stricture (bulbar urethra): 2.0% Urethral stricture (membraneous urethra): 0.8%	Unable to confirm whether majority were high-risk. Outcomes reported included post-operative acute retention, blood transfusion, length of stay, reintervention rate (within 30 days and beyond 30 days reported separately)	Yes (reason for exclusion: “No relevant data”)
14	Trail *et al.* 2021	Retrospective cohort (538)	Prostate volume, median (IQR): 62.5 (45 to 90) cc ASA score 3 or 4: 40.3% Catheter-dependent urinary retention: 40.7% Intermittent self-catheterisation: 3.5%	Unable to confirm whether majority were high-risk.	Published after the systematic review search dates

15	Trujillo *et al.* 2021	Retrospective cohort (587: 381 with prostate volume <80ml, 206 with prostate volume ≥80ml)	<u>Prostate volume <80ml</u> History of anticoagulation: 5.8% History of urinary retention: 26% History of urethral stricture: 10.5% ASA score 3 to 4: 23.5% <u>Prostate volume ≥80ml</u> History of anticoagulation: 6.3% History of urinary retention: 44.3% History of urethral stricture: 5.3% ASA score 3 to 4: 23.9%	>50% high-risk	Published after the systematic review search dates

Appendix C: Ongoing studies

Appendix C1: Completed studies with no publication

Study title, reference	Status, estimated completion	Population (n)	Primary outcome measure(s)	Secondary outcome measure(s)
PRECOCE Study Feasibility Study of Photovaporisation of Prostate With a Limited Length of Catheterization of 3 Hours (NCT02401581)	Completed (no results posted); June 2021	Patients aged between 45 and 80 years old undergoing PVP for LUTS relief (n=200)	Failure rate of limited catheterisation duration of 3 hours; recatheterisation within 24 hours of PVP	Total energy delivered during PVP; duration of recatheterisation
An Open-Label Randomized Phase 4 Study of Greenlight XPS Laser Versus BiVAP Saline Vaporization of the Prostate in Men With Symptomatic Benign Prostatic Hyperplasia (NCT01500057)	Completed, results available on clinicaltrials.gov only	Patients over the age of 18 years undergoing surgical intervention for LUTS symptoms secondary to BPH, AUA ≥15, Qmax <15 mL/s, prostate volume ≥30g, participants randomised to Greenlight XPS PVP (n=31) or BiVAP vaporisation (n=35)	Change in AUA score, Qmax at 12 months	PVR at 12 months
A prospective randomized study comparing PVP, CVP with ThuVAP (UMIN000038914)†	Completed, no results posted; April 2020	Patients aged between 50-100 years, IPSS >7, QoL >1, prostate volume >20ml undergoing surgery for BPH randomised to PVP, CVP and ThuVAP (n=100)	Operation time, temperature and therapeutic effect of symptoms	None reported

Comparing 450nm Diode Laser Vaporization of the Prostate With 532nm Photoselective Vaporization of the Prostate for the Treatment of Benign Prostatic Obstruction—Multi-Center, Single-Blind, Non-Inferiority Design Randomized Controlled Trial (Chinese Clinical Trial Registry: ChiCTR2000032522)†	Completed, no results posted	50-85 years undergoing surgical intervention for BPH, IPSS 8-35, prostate volume 30-100ml, Qmax ≤15 ml/s. Blue laser (Diode laser vaporisation) (n=88) Green Laser‡ (PVP) (n=88)	IPSS, Qmax at 3 months; Hb change post-operatively	Operation time, change in serum electrolytes, time of bladder irrigation, catheterisation time, LoS, QoL, IIEF-5, change in prostate volume, PSA, complications
†Identified by EAC literature search ‡ Intervention is not explicitly defined as GreenLight laser.				

Appendix C2: Ongoing studies

Study title, reference	Status, estimated completion	Population (n)	Primary outcome measure(s)	Secondary outcome measure(s)
Middle Lobe Only Laser Vaporisation or Total Prostate Vaporisation of the Prostate, Prospective Cohort Study (NCT04529369)	Not yet recruiting; October 2030	Patients aged 18-100 years old with LUTS secondary to BPH with predominant middle lobe prostatic adenoma as primary cause of BOO (n=280)	Voiding ability; IPSS; Qmax; PVR; MSHQ-EJD	Efficacy (prostate size, PSA, IPP+/-lateral lobes adenine); additional treatment; bleeding; PVP; erectile dysfunction MSHQ; medication; dysuria
Greenlight Vaporisation vs Xpeeda Vaporesection (NCT04386941)	Active, not recruiting; July 2022	Patients aged 50 years and older undergoing PVP for LUTS relief secondary to BPH (n=97). Prostate volume 40-80ml; IPSS >15; QoL score ≥3; Qmax <15ml/s	IPSS, QoL, Qmax, PVR, PSA changes from baseline to 1, 3, 6 and 12 months	Adverse events; change in prostate volume; IIEF-5 at surgery, 3 and 12 months post PVR
SOAP Trial Multicenter Randomized Open-labelled Trial Which Aims to Show Non-inferiority of Adverse Events Risk During the Maintenance of Oral-anticoagulation in the Surgery of Benign Prostatic Hypertrophy by Laser Photovaporisation (NCT03297281)	Recruiting; May 2022	Patients with BPH who take oral anticoagulants undergoing GreenLight XPS 180 W PVP	Complication rate (up to 30 days post procedure) according to Clavien classification (2 and above) relating to maintenance of anticoagulant use during procedure	Haemorrhagic and thrombotic complications; PVR; PSA; IPSS; ICS; prostatic residual volume; LoS.
CITrUS Study Cotrimoxazole Prophylaxis in Transurethral Resection or Greenlight Laser Vaporisation of the Prostate (NCT03633643)	Recruiting; March 2022	Adult patients aged 18 years and older with obstructive voiding disorder (including BPH and obstructive prostate cancer) undergoing	Incidence of symptomatic UTI treated with antimicrobial agents	Symptomatic UTI, cystitis, epididymitis, pyelonephritis, prostatitis, urethritis; eurosepsis; antibiotic prescription and dosage; asymptomatic bacteriuria; multidrug-

Study title, reference	Status, estimated completion	Population (n)	Primary outcome measure(s)	Secondary outcome measure(s)
Study protocol published; Speich *et al.* 2019		TURP or GreenLight XPS 180 W PVP		resistant bacteria; Clostridium difficile-associated infection; duration of catherterisation; LoS; ICU stay; readmission; change in IPSS and QoL; mortality; adverse events
Comparison photoselective vaporization of the prostate (PVP) with contact laser vaporization of the prostate (CVP) for the benign prostatic hyperplasia (BPH) (UMIN000037088)†	Recruiting; December 2022	Patients aged between 50-99 years inclusive, IPSS >7, QoL >1, prostate volume >30ml (n=200)	QoL	
GreenLight-XPS Laser Vapo-Enucleation versus GreenLight-XPS Laser Vaporization of the Prostate in the Treatment of Symptomatic Benign Prostatic Hyperplasia (ChiCTR1800015867)†	Recruiting; estimated completion not reported	Patients with BPH with one of: urinary retention; hematuria; recurrent UTI; bladder calculi; secondary hydronephrosis; inguinal hernia/severe haemorrhoids or rectocele randomised to two arms, PVEP (n=22) or PVP (n=22)	Qmax, IPSS	PVR, prostate volume, PSA, IIEF, QoL, operation duration, QABq-SF health, ICIQ-SF, bleeding
EPPROSTATECT Ejaculation Preserving Photoselective Vaporisation Versus Plasma Kinetic Vaporisation Versus Transurethral Resection Of The Prostate: A RCT	Unknown; December 2019	Patients aged 50 years and older, prostate volume 30-80g, IPSS>15, QoL <3, Qmax <10 ml/s, sexually active undergoing surgical intervention for LUTS	Ejaculation preservation,MSHQ	Qmax, complications, IPSS

Study title, reference	Status, estimated completion	Population (n)	Primary outcome measure(s)	Secondary outcome measure(s)
(NCT03589196)		secondary to BOO randomised to 3 arms with ejaculation preservation techniques: PVP, PKVP, TURP (n=84)		
Ejaculatory Sparing vs. Non-ejaculatory Sparing GreenLight Laser Photoselective Vaporisation of the Prostate (NCT02749604)	Unknown; March 2018	Patients 50 years and older, ASA ≤3, prostate volume 30-80g, sexually active with the same partner, BOOI ≥20	Ejaculatory function, Ej-MSHQ	BOOI, IIEF-5
Prospective Non-randomized Trial Comparing Holmium Laser Enucleation of the Prostate Versus Greenlight Laser Photoselective Vaporisation of the Prostate in Treating Benign Prostate Hyperplasia in Patients With Bleeding Tendency (NCT02293759)	Unknown; September 2016	Patients 50 years and older undergoing GreenLight XPS 180 W PVP or HoLEP surgical procedure for BPH with perioperative bleeding tendency as defined by low platelet count; INR >1.5; taking antiplatelet or anticoagulant medication (n=60)	Perioperative blood loss	Readmission within 30 days; blood transfusion within 30 days; flow rate at 3 months
Prostatic Artery Embolization Versus 532 nm Green Light Laser Photoselective Vaporisation of the Prostate for Treating Catheter-Dependent Patients With Benign Prostatic Hyperplasia: A Randomised Controlled Clinical Study	Unknown; December 2015	Patients aged 40 to 95 years with BPH with permanent indwelling bladder catheters (n=73)	Voiding ability post catheter removal at 24 hours post PVP	IPSS; reduction in prostate volume; Qmax, change in PVR and PSA

Study title, reference	Status, estimated completion	Population (n)	Primary outcome measure(s)	Secondary outcome measure(s)
(NCT02006303)				
Prospective Registry of Outcomes With the GreenLight Laser System (NCT03736512)	Active, not recruiting; May 2022	Patients aged 40 years and older who underwent GreenLight XPS 180 W PVP (n=30)	IPSS 6 months post PVP	None reported
†Identified by EAC literature search				

Appendix D: Economic literature search

Interface/URL: https://ideas.repec.org/

Database coverage dates: from inception to most recent available on date of search
Search date: 30/11/2021
Retrieved records: 5

Using advanced search interface. Combination of search lines not supported. Searched individually per concept. Time limits applied 2015 to 2021:

Search 1: (greenlight | XPS-greenlight | greenlight-XPS) retrieved 5 results. All assessed on screen for relevancy. None downloaded for further assessment.

Search 2: ((prostatic | prostate) + (hyperplasia | obstruction | hypertrophy | enlargement)) retrieved 29 results. All assessed on screen for relevancy. 5 references downloaded for further assessment.

Search 3: "boston scientific". Retrieved 3 results. All assessed on screen, none downloaded for further assessment

Appendix E: Critical appraisal of the economic evidence

Appendix E1: Economic critical appraisal using CHEERS checklist

Brown *et al.* (2019)

First assessment: RP, QA: RO

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
Title and abstract				
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	Y	"Minimally Invasive Treatment for Benign Prostatic Hyperplasia: Economic Evaluation from a Standardized Hospital Case Costing System"
Abstract	2	Provide a structures summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses) and conclusions.	Y	Purpose, materials and methods, results (base case and uncertainty analysis) and conclusions in abstract. "The purpose of this study was to compare the direct and indirect hospital costs of TURP, PAE and PVP." Perspective and setting assumed to be single Canadian hospital due to author affiliation and that costs were collected in accordance with Ontario Case Costing Initiative.
Introduction				
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	Y	"The overall BPH cost of care in the USA is estimated to be in between $2.3–4 billion per year, and around 20,000 surgical treatments for BPH are performed per year in Canada"; "These minimally invasive alternatives to TURP have the potential to reduce costs and resource utilization at the hospital level. The purpose of this study was to analyze the costs of PAE, PVP and TURP in patients with BPH. To our knowledge, there are no published economic evaluations of PAE, PVP and TURP together."
Methods				
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	Y	"A chart review was performed in patients who underwent TURP, PVP and PAE from April 2015 to March 2017. The time period was chosen as this

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
				represents the beginning of our PAE experience." Patient characteristics described in Table 1.
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	Y	Setting not explicitly reported but "The research ethics board (REB) at our institution approved this retrospective chart review study", so assumed to be Toronto General Hospital due to ethical board approval (University Health Network) and lead author affiliation.
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	Y	Perspective not explicitly reported, but costs were obtained from the finance department of the treating institution in accordance with Ontario Case Costing Initiatives (standardised medical case costing system for Ontario hospitals), so assumed to be single Canadian hospital.
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	Y	Two interventions were compared with TURP due to comparable clinical outcomes and fewer complications. "To our knowledge, there are no published economic evaluations of PAE, PVP and TURP together."
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	Partly	Retrospective analysis of "costs incurred from the time of admission to subsequent discharge as well as costs related to any re-admissions within 30 days of the procedure." Short time horizon not justified, though likely to be because of difficulty following up over longer period, or expectation of no further cost incurrence in this time.
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	N/A	Retrospective analysis of incurred costs, so discounting not appropriate..
Choice of health outcomes	10	Describe hat outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	Y	Outcomes not reported as measure of benefit. Direct and indirect costs were considered within the study, and breakdown of costs reported for pre-admission, operating room and angiography suite, anaesthetic,

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
				post-anaesthesia care and medical imaging, inpatient, and pharmacy, costs.
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	Partly	Study design clearly reported. Use of single study not justified, but due to retrospective nature, assumed to be pragmatic.
	11b	*Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	N/A	
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	N/A	
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Y	"Cost data for each procedure and related inpatient hospital care costs were provided by the finance department of our institution—these include costs incurred from the time of admission to subsequent discharge as well as costs related to any re-admissions within 30 days of the procedure." Authors report micro-costing approach was used.
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	N/A	
Currency, price, date and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base	Y	"The study took place in Canada, and therefore all economic data were obtained in CAD ($). Subsequently, all quotations were converted to US dollars (US$), with US-$1 equivalent to $1.2986, with regard to the annual exchange rate in 2017".

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
		and the exchange rate.		
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	N/A	Hospital resource costing study, no decision-analytical model used.
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	N/A	No decision-analytical model used.
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	Y	"Probabilistic sensitivity analysis was performed using Monte Carlo simulation with 10,000 random samples. This analysis was performed to account for parameter uncertainty and helps to explore optimal strategy distribution. The model was built using gamma distributions."
Results				
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	Partly	Unit costs for each parameter not reported, only overall total costs and breakdowns. Authors report using gamma distributions for PSA, but reasoning not justified.
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	Y	Table 1 shows mean overall costs, standard deviations, ranges and interquartile ranges; Table 2 shows the mean hospital costs and standard deviations, broken down by hospital cost centres; Figures 2 and 3 show general, and patient specific variable direct and indirect costs in box plots across the three interventions. Figure 4 shows PSA of the three strategies across simulation sampling. ICERs not applicable, therefore not reported.
Characterising uncertainty	20 a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together	N/A	Incremental costs and effectiveness not applicable.

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
		with the impact of methodological assumptions (such as discount rate, study perspective).		
	20 b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	N/A	
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost- effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	N/A	Subgroups not reported.
Discussion Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	Partly	Authors conclude "Our study results demonstrate that PAE is significantly less expensive than both PVP and TURP in terms of total costs. These costs differences are driven by the indirect costs of surgery and should be considered by hospital decision makers when comparing the cost of these alternative treatments for BPH." Authors acknowledge study "…is limited by a relatively small sample of PAE and PVP patients and this reflects real-world practice and the availability of alternatives for BPH." Authors acknowledge their practice may differ to other centres, in their use of different post-operative observation stay settings: post-anesthesia care unit, medical imaging day unit, surgical short stay unit and inpatient ward. Further limitations and generalisability not explicitly addressed.
Other Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	N	Funding source not reported.

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	Y	"The authors declare that they have no conflict of interest."

Caicedo *et al.* (2019)

First assessment: RP, QA: RO

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
Title and abstract				
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	Y	"Photovaporization of the prostate with GreenLight™ laser 180 W XPS versus transurethral resection of the prostate with monopolar energy for the treatment of benign prostatic enlargement: a cost-utility analysis from a healthcare perspective"
Abstract	2	Provide a structures summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses) and conclusions.	Y	Objectives, perspective, setting, participants, intervention, design, data sources (specific inputs not reported), outcome measures, base case results, and conclusions all reported in abstract. Results of uncertainty analysis not reported in abstract.
Introduction				
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	Y	Authors report increasing life expectancy with low adherence to medical therapy within the relevant population thus anticipating a rise in number of patients requiring intervention. Open prostatectomy is widely used, however is associated with high complication rates and bleeding. Authors recognise American and European guidance includes TURP and PVP as surgical intervention options and that there is evidence to suggest lower complication rates and bleeding particularly in high risk patients and may be associated with a shorter stay. The study aimed to evaluate the cost-utility ratio of GL-PVP with monopolar TURP in those with moderate to severe LUTs in terms of symptom improvement and QALYs from Colombian healthcare perspective.
Methods				

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	Partly	Base case population characteristics reported; >50 years, IPSS ≥10, normal PSA, Qmax ≤15, and no subgroups analysed.
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	Y	Assumed to be "high-complexity local hospital" as this was the setting used to inform resource use.
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	Y	"Healthcare perspective in Colombia" with utilities taken from published literature "assuming that the population characteristics are different from the Colombian population" [the EAC assumed this was an error and that the characteristics were assumed not to be different]. Costs for each health state used in the model "taken from clinical records based on the frequency and resource use of a high-complexity local hospital"
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	Y	PVP vs monopolar TURP interventions selected for cost-utility ratio evaluation due to possible benefits of shorter hospital stays and "lower costs for the healthcare system". Four health states used in Markov model described in Figure 1 and source data described in Table 1.
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	Y	"A 2-year time horizon was defined with four cycles of 6 months each, according to the best evidence available." Data was taken from the only multicentre RCT (Thomas *et al.* 2016) with no studies identified with over 2 years of GL-PVP XPS 180 W follow up data available.
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	Y	"A 5% discount rate was used during the 2-year time horizon, using a range of 0-10% in the sensitivity analysis, according to standard of care recommendations"
Choice of health	10	Describe what outcomes were used as the	Y	"The model's effectiveness parameters were taken from

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
outcomes		measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.		the literature, specifically from the only multicenter randomized clinical trial published in European Urology by Thomas *et al.* in 2016, which is known by the urological community as the GOLIATH study" and validated by a panel of four experts. QALYs were used, based on the "utilities of the available literature" and specified in Table 1.
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	Y	The GOLIATH RCT is "considered by experts as the best available evidence on the subject to date."
	11b	*Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	N/A	
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	Y	QALYs taken from literature, no preferences elicited.
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	N/A	
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Partly	"The costs included in the model correspond to each health state (asymptomatic, medical management, re-operation and re-intervention), as well as to each surgical procedure (PVP and M-TURP)" … "we used clinical records from the public healthcare system cost list, a high-complexity local hospital, hospital bills, opinion of experts and the literature review. Direct costs

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
				of surgical interventions were included." Unit costs not reported.
Currency, price, date and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	Y	"The unit of measurement corresponds to Colombian pesos (COP) converted to US dollars (USD) according to the official exchange rate (1 USD=2947.85 COP, May 1st 2017)". No adjustment to current year required.
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	Partly	Markov model used with Figure 1 demonstrating the structure. Reason for model choice not reported.
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	Y	Model assumptions described in their own section.
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	Y	Authors used both deterministic and probabilistic sensitivity analysis to address uncertainties. Probabilistic analysis used a Monte Carlo simulation with a hypothetical cohort of 1,000 patients=.
Results				
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	Partly	No parameter values reported, except utilities in Table 1. In terms of sensitivity analysis "For costs, a triangular distribution was assigned, and for the probabilities and utilities, a beta distribution was used" but no source or justification given.
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	Y	"In our study, PVP was more cost-effective than M-TURP, gaining 1.81 and 1.59 QALYs, respectively. The cost of the most effective alternative was US$7777.59, which represents US$979.62 more than the conventional surgery (US$6797.98). These results indicate an incremental cost effectiveness ratio of US$4452.81 per QALY, suggesting that PVP is a cost-

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
				effective alternative with the current willingness-to-pay in Colombia (Fig. 2)."
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	N/A	
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	Y	Tornado diagram presented in Figure 3. Results also reported in the narrative for deterministic and probabilistic sensitivity analysis.
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost- effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	N/A	No subgroup analysis.
Discussion Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	Y	"PVP using GreenLight™ laser 180 W XPS compared to M-TURP is the most effective strategy, but also the most costly option in the Colombian context. According to the willingness-to-pay in Colombia per QALY and controlling the uncertainty of the parameters of the model, in all cases the PVP was cost-effective." "However, it is important to highlight the main limitation of our study, which is the lack of reported utilities in the Colombian population. Also, although mid-term effectiveness outcomes for PVP in Colombia are reported in the literature, there is a lack of long-term effectiveness parameters for both PVP and M-TURP." Discussion of available evidence from other countries; Spain, UK and China. "Additionally, we need to

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
				consider the sustainability of implementing this intervention as a recommended clinical practice taking into account a budget-impact analysis according to disease prevalence, technology characteristics, availability and costs in other regions of our country"
Other				
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	Y	"We received financial support from Boston Scientific Corporation (ISRURO00005)." Role of funder not explicitly stated. Authors' contributions clearly stated and some of the authors have affiliations with funder.
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	Y	"The authors Juan Ignacio Caicedo, Mauricio Plata and Carlos Gustavo Trujillo declare to have served as instructors of the technique of PVP with GreenLight™ laser 180 W XPS in Colombia through the Company Gilmedica and Boston Scientific Corporation. Darío Londoño, Alejandra Taborda, Jonathan Campos, Juan Guillermo Cataño, Cristina Domínguez, Daniela Robledo and Alejandra Bravo declare no conflicts of interest related to the present study."

Erman *et al.* (2018)

First assessment: RP, QA: RO

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
Title and abstract Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	Y	"Pharmacotherapy vs surgery as initial therapy for patients with moderate-to-severe benign prostate hyperplasia: a cost-effectiveness analysis"
Abstract	2	Provide a structures summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses) and conclusions.	Y	Objective, perspective, study design, results (including base case and sentence summarising probabilistic analysis), and conclusions reported in abstract. Setting not explicitly reported in abstract, and model inputs not reported other than to say "model was populated using published literature".
Introduction Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	Y	Authors acknowledge BPH as a common condition affecting up to 50% of men aged 50 years and older and that several treatment options exist for patients depending on the severity of the condition and related symptoms. Authors identify that pharmacological interventions, which are often the first line of intervention, may not resolve symptoms, are long-term treatments, and may be more costly over the patient lifetime compared to early surgical intervention. "The objective of the present study was to evaluate the cost-effectiveness of using a BPH surgery, such as TURP or GLPVP, as initial treatment for men with moderate-to-severe BPH-LUTS compared to the standard practice of using pharmacotherapy as initial treatment followed by a BPH surgery if symptoms do not resolve."
Methods				

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	Y	Baseline characteristics of hypothetical simulated patients specified in text and Table 1, and based on published evidence. “The target population was men with a mean age of 65 years, with moderate-to-severe LUTS with presumed benign prostatic enlargement referred to a urologist with no presumed contraindications for medical or surgical therapy. The mean prostate volume of the patients in our hypothetical cohort was 53 mL, the mean IPSS was 16, and the mean PSA level was 3.8 ng/mL, based upon patient characteristics of referenced clinical trials.” No subgroups described.
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	Partly	Assumed to be Urology service of Toronto Western Hospital, Ontario, but not explicitly stated in text.
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	Y	“Cost-effectiveness analysis was performed from a public payer perspective”. “Cost-effectiveness was determined using a conventional willingness to pay threshold (k) of $50 000 (Canadian dollars)/QALY gained”
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	Y	We evaluated the cost-effectiveness of pharmacotherapy (5-ARI, a-blocker, 5-ARI + a-blocker) followed by delayed surgical therapy (GL-PVP or TURP) for patients who failed the initial treatment vs upfront surgical therapy (GL-PVP or TURP). In total, eight strategies were compared: ...” Reason for selection not explicit although consistent with outcomes and study aims.
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	Y	”Lifetime horizon” reported. Not explicitly justified although assumed to be due to the comparator (pharmacotherapy) being associated with lifelong use.
Discount rate	9	Report the choice of discount rate(s) used for	Y	Reported “All future costs and benefits were discounted at 1.5% annually…” and cited the Canadian Agency for

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
		costs and outcomes and say why appropriate.		Drugs and Technologies in Health's Guidelines for the Economic Evaluation of Health Technologies.
Choice of health outcomes	10	Describe hat outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	Y	"The outcomes were discounted costs, quality-adjusted life years (QALYs), and incremental cost-effectiveness ratios (ICER)."
Measurement of effectiveness	11 a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	N/A	
	11 b	*Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	Partly	"Clinical probabilities including clinical effectiveness with respect to IPSS improvement and the probability of adverse events were obtained from large randomised trials and meta-analyses", and sources identified in Table 1,. Methods of literature identification and synthesis not explicitly reported, but exclusion criteria stated in Table 1.
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	Y	Methods of establishing utilities well described, including use of standard gamble method for utility associated with adverse events. No other preference elicitation indicated, and population not reported.
Estimating resources and costs	13 a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	N/A	
	13 b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states.	Y	Clinical and cost sources obtained from published literature and "a retrospective cost analysis conducted

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
		Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.		between September 2013 and 30 September 2015". Unit costs listed in supplementary material, Table S3.
Currency, price, date and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	Partly	"Where available Canadian sources were used. For non-Canadian sources, costs were converted to Canadian prices using purchasing power parity. All costs were inflated to the 2015 cost year using the consumer price index." Exchange rate not reported.
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	Partly	"A microsimulation decision-analytic model was developed in TreeAge Pro 2018 (TreeAge Software Inc., Williamstown, MA, USA)", with model structure shown in Figure 1. Justification for using model not reported.
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	Y	"A cycle length of 3 months was used, as it is the period over which symptoms and adverse events may resolve. A microsimulation sample size equating to 250 000 patients was determined empirically by running iterations of the model with 100 to >500 000 simulated individuals until model outputs stabilise." Assumptions for disease progression, treatment adherence and relapses also clearly reported and supported by published literature.
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	Y	Scenario analysis, threshold analysis, and probabilistic (Monte Carlo) analysis all reported.
Results				

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	Y	Baseline patient characteristics, including mean (SD) values, ranges and distributions reported and referenced in Table 1. Input values, ranges, probability distributions, and references, for clinical parameters, utilities and costs, clearly reported in supplementary Tables 1-3.
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	Y	Discounted costs, QALYs and ICERs reported clearly in Table 2 and undiscounted costs, QALYs and ICERs reported in Supplementary Tables S5. "Upfront GL-PVP cost $1700 more and resulted in an average gain of 0.12 QALYs compared to the next most effective strategy, which was upfront combined treatment followed by delayed GL-PVP (ICER: $14 069/QALY). Whilst, the most effective strategy, upfront TURP, cost $1015 more and resulted in only a small gain of ~0.03 QALYs in comparison with the second most effective option, which was upfront GLPVP (ICER: $29 066/QALY)."
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	N/A	
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	Y	Results of sensitivity analysis, threshold analysis and probabilistic analysis reported in the text, and in supplementary material (Tables S6 and S7, and Figures S2 and S3).
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost- effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or	N/A	No subgroups reported.

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
		other observed variability in effects that are not reducible by more information.		
Discussion Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	Y	"compared to upfront pharmacotherapy, upfront surgeries were more costly but also more effective. In addition, all pharmacotherapy strategies involving delayed TURP for those who fail initial therapy were dominated." and the authors concluded "that using delayed GL-PVP instead of TURP for patients that fail initial pharmacotherapy is economically more attractive." Limited discussion of generalisability, but did discuss results in context of other previous economic evaluations performed in Canada. Authors acknowledge limitations including use of clinical effectiveness and adverse event data from randomised trials and meta-analyses, and that this may not be representative of real-world patients, lack of direct comparison between BPH surgery and pharmacotherapy, and that the ICER "is likely to be influenced by the accuracy of the estimates of treatment effects, costs, and the natural history of IPSS progression…". Authors acknowledge that although they used sensitivity analysis, they did not consider the possibility of switching pharmacotherapy agent for those failing the first option, the cost of purchasing and maintaining technology, patient risk preference, budget impact, and impact of the necessary withdrawal from medication prior to TURP. An additional comment was that only one surgical intervention for BPH was considered despite others being available.
Other Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	Partly	"The research was funded by an unrestricted educational grant from Boston Scientific." Role of funders not explicit.

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	Y	"Dr Elterman reports grants from Boston Scientific, during the conduct of the study; grants and personal fees from Astellas, grants and personal fees from Boston Scientific, personal fees from Medtronic, grants and personal fees from Pfizer, personal fees from Ferring, and personal fees from Acerus, outside the submitted work. All other authors have nothing to disclose."

Masucci *et al.* (2018)

First assessment: RP, QA: RO

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
Title and abstract				
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	Y	"Cost analysis of Greenlight photoselective vaporization of the prostate compared to transurethral resection of the prostate for benign prostatic hyperplasia"
Abstract	2	Provide a structures summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses) and conclusions.	Y	Objectives, perspective, setting, methods, base case results (no uncertainty analyses conducted) and conclusions reported in abstract.
Introduction				
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	Y	Authors identify prevalence of BPH and impact of associated symptoms on QoL. GreenLight PVP identified as an alternative treatment option to TURP with possible benefits in shorter hospitalisation, symptomatic improvement and decreased morbidity. "The objective of our study was to compare the costs of Greenlight PVP vs. TURP and bipolar TURP from a hospital perspective, as well as to determine the predictors of total cost."
Methods				
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	Y	Patient characteristics described in Results and presented in Table 1. Included "patients who underwent Greenlight PVP, TURP, or bipolar TURP". "…the first 10 cases of Greenlight PVP for each physician were excluded from the analysis" and "patients presenting through the emergency department were also excluded due to the learning curve of using the new technology." No subgroups reported.
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	Y	Assumed to be Division of Urology of Toronto Western Hospital, Ontario.

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	Y	"Costs were captured from the perspective of the hospital. For each patient, both direct and indirect hospital costs were obtained for each procedure."
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	Y	Interventions reported as GreenLight PVP, TURP and bipolar TURP. Justification for these being chosen not reported explicitly, but assumed to bebased on published evidence suggesting comparable symptom relief, improved safety, morbidity, length of hospital stay and costs.
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	Partly	Assumed to be 60 days, as "number of readmissions at 30 and 60 days post-intervention were obtained from the Toronto Western Hospital administrative database." but appropriateness not reported.
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	N/A	Costing study only, no modelling, discount rates not applicable.
Choice of health outcomes	10	Describe hat outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	Partly	Outcomes not explicitly defined, but main outcomes assumed to be readmissions at 30 and 60 days. Number of visits, proportions of procedures completed as an inpatient or outpatient, length of stay, and time spent in the operating room, also reported.
Measurement of effectiveness	11 a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	Partly	Study design well reported. Justification for sufficient data not reported, but as a retrospective costing study, assumed to be pragmatic. Authors acknowledge limited generalisability to other settings within discussion.
	11 b	*Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	N/A	

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	N/A	No outcome preferences elicited.
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	N	” For each patient, both direct and indirect hospital costs were obtained for each procedure”. Costed items listed, but unit costs not reported.
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	N/A	
Currency, price, date and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	Y	“Costs were based on surgeries conducted between September 2013 and September 30, 2015 at the Toronto Western Hospital, Toronto, Ontario”. Costs were all reported in 2015 Canadian dollars with no conversion or adjustments reported.
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	N/A	Costing study, no decision-analytical model used. However, ”Multiple linear regression analysis was performed in order to identify predictors of total cost and obtain covariate-adjusted costs.”
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	N/A	No decision-analytical model used.
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data;	N	Not reported

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
		approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.		
Results				
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	N	Unit costs for each parameter not reported, only overall total costs and breakdowns of variable and fixed, and direct and indirect costs, and breakdowns by inpatient and day-case procedures, and readmission timescales (if applicable). ..
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	Y	Mean costs per patient, including 95% Cis, for each intervention reported in Tables 2-5.
Characterising uncertainty	20 a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	N/A	Incremental costs and effectiveness not applicable.
	20 b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	N/A	
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost- effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	Partly	Mean total costs per patient per procedure reported separately for those undergoing interventions as a day-case, and as an inpatient. Cost differences were also reported following adjustments for covariates. Authors acknowledge a difference in anticoagulation therapy status at baseline between groups, but p values and subgroup analysis not reported.

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
Discussion Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	Y	"Given comparable patient safety and quality of life outcomes for both treatments, whether Greenlight PVP should be adopted as an alternative to TURP may be a matter of cost. We found that Greenlight PVP cost $1142 less than bipolar TURP and $1127 less than TURP. The savings in costs are mainly attributed to costly inpatient hospitalizations associated with TURP" which supports conclusion that Greenlight PVP is "a preferable option for the hospital." Limitations of study identified as being that only hospital costs were considered (no patient costs or costs incurred by Ministry of Health and Long-Term Care), no costs were included for follow up procedures although readmissions were considered, and results from the single centre study may not be generalisable to other settings: Authors report the findings to be consistent with other published literature.
Other Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	N	No source of funding reported.
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	Y	"The authors report no competing personal or financial interests."

Mathieu *et al.* (2017)

First assessment: RP, QA: RO

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
Title and abstract				
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	Y	"Perioperative and economic analysis of surgical treatments for benign prostatic hyperplasia: A study of the French committee on LUT"
Abstract	2	Provide a structures summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses) and conclusions.	Partly	Objectives, perspective, setting, study design, base case results, and conclusions reported. Model inputs not reported, and no uncertainty analysis carried out..
Introduction				
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	Y	Authors note high prevalence of LUTS due to benign prostatic obstruction (BPO), and that "New [surgical] techniques may be associated with an increased cost in terms of equipment and consumables use. However, these additional costs may be balanced by shorter hospital stay and other improvements in perioperative care. The objective of this study was to assess perioperative cost related to surgical treatment of BPO."
Methods				
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	Y	Table 2 reports the patient characteristics. Patient selection justified as "In each center, data from 20 to 30 consecutive patients who underwent a surgical treatment for LUTS related to BPO between January 2012 and June 2013 were collected". . No subgroups reported.
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	Y	Table 1 reports the institution practice and characteristics. "Nine academic or private institutions in France participated in this retrospective study."

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	Y	"The outcome of each technique was assessed in terms of cost from the institutional perspective. Short-term hospital costs were evaluated for each procedure using the National costs study 2010 [which] defines for different procedures and groups of patients (groupes homogènes de malades [GHM]), variables costs and fixed costs related to the LOS"
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	Y	Authors acknowledge TURP and OP as accepted standard of care with newer techniques (PVP, HoLEP, ThuLEP) being shown as safe and effective alternative treatments with limited data for cost-effectiveness.
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	Partly	Time horizon not reported, but assumed to be the period of hospitalisation only as "The objective of this study was to assess perioperative cost related to surgical treatment of BPO" and long term costs and consequences not reported.
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	N/A	Costing study only, so discounting not applicable.
Choice of health outcomes	10	Describe hat outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	Y	Only outcome related to cost was mean cost of hospitalisation, but clinical outcomes included mean operative time, mean operative time per gram of prostate, mean and median length of stay, mean length of stay for prostates less than 80 ml and not less than 80 ml.
Measurement of effectiveness	11 a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	Partly	Study design well reported. Justification for sufficient data not reported, but as a retrospective costing study, assumed to be pragmatic.

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
	11 b	*Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	N/A	
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	N/A	No preferences elicited.
Estimating resources and costs	13 a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Y	"In our study, for each hospitalization, variables costs were conserved and fixed costs were recalculated by the ratio between observed LOS and mean national LOS. In NCS, only cost related to OP and TURP are considered. For PVP and ThuLEP/HoLEP, we considered variables and fixed costs used for TURP. Cost of equipment and single-use disposal … were estimated according to the manufacturer charge policy." Formula for calculating total cost provided.
	13 b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	N/A	
Currency, price, date and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	Partly	"Costs were evaluated for each procedure using the National costs study 2010 from French technical agency of information on hospitals (ATIH; Agence technique de l'information sur l'hospitalisation) database". Costs reported in EUR (€) and no adjustment to current year or currency conversion performed.

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	N/A	N/A – no decision analytical model. Cost minimisation analysis used, with short term outcomes costed from retrospective data.
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	Y	"For modelization purposes, we assumed that short-term functional results after each procedure were entirely similar, based on available data from the literature." "We assumed that for PVP one fiber was used per patient and that for LEP, one fiber was used for twenty procedures."
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	Partly	Methods for statistical analysis reported, including χ^2 tests, analysis of variance, and logistic regression.
Results				
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	Partly	Patient characteristics reported in Table 2 and perioperative characteristics reported in Table 3. Input cost values not explicitly stated.
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	Partly	Table 4 shows the mean cost of hospitalisation per procedure, stratified by prostate volume. Also reported in text.
Characterising uncertainty	20 a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions	N/A	Retrospective costing study, no characterisation of uncertainty required.

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
		(such as discount rate, study perspective).		
	20 b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.		
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost- effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	Y	Authors report on the impact of a larger prostate on perioperative and LoS costs, and as a predictor of complications. Table 4 stratifies mean cost of hospitalisation by prostate volume.
Discussion				
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	Y	Authors acknowledge that their finding "PVP and HoLEP are associated with a shorter length of stay than TURP or OP" is not consistent with a recent meta-analysis, and suggest potential reasons. Limitations reported included the study's retrospective nature, estimation of costs and resource use due to scarcity of data, lack of data around the skills and experience levels of the surgeons and any impact this may have, and that only costs incurred during the first hospitalisation were considered (that is, no readmission costs were included). The authors concluded "…these procedures could be cost-effective alternatives to OP. However, the mean LOS we observed in our study is still not sufficient to consider that these procedures are cheaper or more cost effective than TURP for prostate less than 80 mL"
Other				
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	N	Funding for work not reported.
Conflicts of interest	24	Describe any potential for conflict of interest of	Y	"R. Mathieu: support for Congress by AMS; S. Lebdai: no; J.N. Cornu: consultant for companies,

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
		study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.		Allergan,Astellas, Boston Scientific, Bouchara-Recordati, Coloplast, Medtronic, Mundipharma, Pfizer, SAP, Takeda and investiga-tor for Astellas, Cousin Biotech, Coloplast, GT Urological,Ipsen and Medtronic; A. Benchikh: no; A.R. Azzouzi: no; N.B. Delongchamps: no; O. Dumonceau: no; A. Faix:no; M. Fourmarier: trainer for Company EDAP-TMS and Boston Scientific; O. Haillot: not stated conflict of interest; B. Lukacs: lecturer for Mylan; V. Misrai: trainer for Boston Scientific; A. de la Taille: no; G. Robert: trainer for CompanyEDAP-TMS and Lumenis; A. Descazeaud: no.”

Ulchaker and Martinson (2018)

First assessment: RP, QA: RO

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
Title and abstract				
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	Y	"Cost-effectiveness analysis of six therapies for the treatment of lower urinary tract symptoms due to benign prostatic hyperplasia"
Abstract	2	Provide a structures summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses) and conclusions.	Y	Objective, perspective, study design and inputs, results and conclusions included. Setting and location not specified, but assumed to be USA due to author affiliation and cost reporting in dollars. Base case results not reported in detail, and no results of uncertainty analysis provided.
Introduction				
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	Y	Authors acknowledge BPH is a common and chronic condition that requires high US health care resources, and that "drug adherence rates are often low" and are "expensive over long periods of time". "…purpose of this cost-effectiveness analysis is to examine critical positioning of treatments for LUTS/BPH in the marketplace and the best use of health care funds and quality-of-life benefits for the patient in the US." The health policies of AUA and EUA guidelines for the management of BPH are referenced.
Methods				
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	Partly	Base case patient characteristics reported only as "all patients were assigned the same baseline score in the model (IPSS of 22) to make the comparisons among therapies as fair as possible. The standard deviation (SD) of means from individual studies was used in the probabilistic sensitivity analysis."

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	N	Not explicitly stated, but assumed to be Department of Urology in US hospital.
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	Y	"Costs and cost-effectiveness were analyzed over 2 years from the perspective of the health care payer.", and costs used from Medicare.
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	Partly	Six therapies defined and identified from those recommended in AUA and EUA guidelines for management of BPH although reason for selection not explicit.
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	Y	"The base-case timeframe of 2 years was selected to encompass the limited post-treatment follow-up times of 2 years for some of the MITs included in the analysis. The authors acknowledge that longer-term results are important to all stakeholders, but for most BPH therapies, the short-term trends have been consistent with longer-term results."
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	Partly	"Costs and effects were discounted at 3%." Reasons unspecified.
Choice of health outcomes	10	Describe hat outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	Y	Outcomes reported as change in IPSS, return of LUTS, adverse events (incontinence, *de novo* erectile dysfunction, stricture, contracture, stenosis, acute urinary retention, urinary tract infection). Relevance not explicitly justified, but assumed to be to support reporting of cost effectiveness.
Measurement of effectiveness	11 a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	N/A	

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
	11 b	*Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	Y	Literature search methodology for data sources including the use of MeSH terms, and methods for synthesising clinical effectiveness data, reported.
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	N/A	QALYs not used as measure of effectiveness, so outcome preferences not elicited from individuals.
Estimating resources and costs	13 a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	N/A	
	13 b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Y	Unit costs and resource use well reported and sourced as from published literature and expert opinion.
Currency, price, date and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	Partly	Authors report using costs and resource quantities from 2016 (Medicare national average fee schedules; Federal Upper Limit payments) and 2014 sources (Medicare MEDPAR; Medicare Part D prescriber data), but do not report adjusting to current year. Exchange rates assumed not applicable due to local currency being used (USD $).
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	Y	Markov model used with structure shown in Figure 1.

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	Y	Many assumptions reported. “The non-resolving ED and some incontinence were assumed to be permanent and need chronic therapy…AUR was assumed to be due to either disease progression or a stenosis and treated accordingly.” “For the modelling, it is assumed that ComboRx is the typical first line of treatment for LUTS/BPH. Patients who have inadequate symptom relief or worsening of LUTS may progress to one of the three MIT options (0.33 assumption). Patients who progress after an MIT have two surgical options (0.5 assumption).”
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	Y	Analytical methods well described. “Uncertainty was evaluated using a probabilistic sensitivity analysis in which IPSSs used normal distributions and rates per cycle used beta-binomial distributions.”
Results				
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	Y	Model input values provided in Tables 1 and 2, with references, and in terms of sensitivity analysis “IPSSs used normal distributions and rates per cycle used beta-binomial distributions.”
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	Y	Cost effectiveness simulations and ICERs of interventions shown in Table 3 and Figure 2.

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	N/A	
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	Y	"Simulations include the probabilistic sensitivity analysis, so they include the uncertainty in the estimates of effects and rates". CEACs in Figure 3 summarise probabilistic sensitivity analysis results, and results well reported in text.
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost- effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	Partly	Authors do not report any subgroup analysis but acknowledge the limitation that "…the sample of patients assessed is heterogeneous; the analysis represents the continuum of care that a patient may experience based on variables such as degree of symptom bother, tolerance, prostate size or comorbidities, and therapeutics available to them".
Discussion				
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	Y	Key findings summarised in discussion, linked to other evidence, and linked to conclusions "The medication option is the least expensive but not cost-effective as this modality requires extended use to barely achieve half the urinary symptom improvements obtained through minimally invasive procedures…Greenlight PVP and TURP provide similar and greater symptom relief; however, these options also demonstrate higher rates of AEs and increased procedure time, and potentially require general/spinal anesthesia, adding additional costs to the payer…" The authors acknowledge limitations, including heterogeneity of included patients, and small sample sizes and short follow up duration in the literature used to support the modelling. Generalisability not addressed.

Section/item	#	Recommendation	Reported (Y/N)	Additional comments
Other				
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	Y	"This study was supported by NxThera, Inc., Maple Grove, MN, USA. The study results have not been contingent on the sponsor's approval nor has the sponsor been involved in censorship of the report."
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	Y	"Dr. Ulchaker participated as a clinical investigator in the pivotal trial of the convective RF water vapour thermal therapy. Dr. Martinson of Technomics Research was contracted to perform the cost-effectiveness analysis. The authors report no other conflicts of interest in this work."

Appendix E2: Critique of Company *de novo* model (Drummond checklist 1996)

First assessment: RP, QA: KK

	Judgement				
Item	**Yes**	**No**	**Not clear**	**Not appropriate**	**EAC comment**
Study design					
1*. The research question is stated.	X	¨	¨		"The objective of this preliminary analysis is to compare the cost of treating high-risk patients referred for BPH surgery with GreenLight compared to other surgical options offered to high-risk patients in the National Health Service (NHS)." Comparators reported as TURP and HoLEP in line with published scope. Modelling high-risk patients only is a relevant subgroup to be considered (as listed in the Final Scope).
2*. The economic importance of the research question is stated.	¨	X	¨		Importance for the economic modelling is not reported.
3*. The viewpoint(s) of the analysis are clearly stated and justified.	X	¨	¨		"Costs are considered from an NHS payer perspective" (in line with scope).
4*. The rationale for choosing alternative programmes or interventions compared is stated.	X	¨	¨		"GreenLight was selected as the intervention and compared to TURP and HoLEP, both of which are expected to be offered to high-risk patients in the NHS."
5*. The alternatives being compared are clearly described.	¨	X	¨		No additional description of the comparators was provided. TURP aggregates results from mono- and bi-TURP (25/75 split).
6*. The form of economic evaluation used is stated.	X	¨	¨		"Cost-minimisation analysis"
7*. The choice of form of economic evaluation is justified in relation to the questions addressed.	¨	¨	X		Not explicitly stated. Authors refer to two prior cost-minimisation economic models that have been submitted for NICE economic evaluation that include GreenLight. The intervention is available following previous NICE evaluation, so model choice is considered justified. Authors report a justification for the choice of model (Markov

Item	Judgement				EAC comment
	Yes	No	Not clear	Not appropriate	
					model over prior decision tree) including the ability to capture hospital costs more accurately for high-risk patients, improved calculation of adverse events, use updated costs, and ability to select multiple comparators and different interventions.
Data collection					
8*. The source(s) of effectiveness estimates used are stated.	X	¨	¨		Costs associated with retreatment considered. Safety outcomes include length of stay and short-term (severe and non-severe) and long-term adverse events. The Company later included scenario analysis relating to erectile dysfunction outcomes.
9. Details of the design and results of effectiveness study are given (if based on a single study).	¨	¨	¨	X	Cost-minimisation analysis. Retreatment rates sources from multiple studies (the GOLIATH RCT compared GreenLight to TURP, but there is additional no randomised evidence identified which compared GreenLight to HoLEP).
10. Details of the methods of synthesis or meta-analysis of estimates are given (if based on a synthesis of a number of effectiveness studies).	¨	¨	X	¨	Some clinical parameters included in high-risk model were taken from an unpublished systematic review submitted by the Company as part of clinical submission; values derived from synthesised data with primary sources for each parameter not explicitly reported. Cost parameters taken from a prior MTG49 (Rezum). Information sources described in excel document and within Table 2 of the updated Company economic submission. The Company also included a single study source for inputs relating to erectile dysfunction; however, the source did not include two of the interventions (GreenLight and HoLEP) and the Company assumed equivalence with other procedures without providing justification or supporting evidence.
11*. The primary outcome measure(s) for the economic evaluation are clearly stated.	X	¨	¨		"The results report costs per patient treated with GreenLight XPS, Mono-TURP, Bi-TURP, and HoLEP over 5 years". The EAC asked the Company for clarification regarding the time horizon as outcomes reported at 5 years despite the model and methods defining a time horizon of 4 years.
12. Methods to value benefits are stated.	¨	¨	¨	X	N/A – cost-minimisation analysis.

Item	Judgement				EAC comment
	Yes	No	Not clear	Not appropriate	
13. Details of the subjects from whom valuations were obtained were given.	¨	¨	X	¨	All clinical parameters taken from unpublished systematic review submitted by the Company as part of clinical submission; values derived from synthesised data with primary sources for each parameter not explicitly reported. The Company updated figures from the original submission following the EAC identifying errors within the values used and referred. Errors persisted following changes by the Company as highlighted by the EAC.
14. Productivity changes (if included) are reported separately.	¨	¨	¨	X	N/A (not included)
15. The relevance of productivity changes to the study question is discussed.	¨	¨	¨	X	N/A (not included)
16*. Quantities of resource use are reported separately from their unit costs.	X	¨	¨		Model inputs and values described in Tables 2-4. Resource use for high-risk patients taken from unpublished systematic review submitted by the Company with primary sources not explicitly reported. Unit costs not explicitly reported in narrative summary, available in excel model.
17*. Methods for the estimation of quantities and unit costs are described.	¨	¨	X		Unit costs and sources available in excel model. Parameters influencing qualities taken from unpublished submitted systematic review by Company with primary sources not explicitly reported. The Company updated their submission to include costs associated with the use of saline bladder irrigation with TURP, the source costs are not explicitly reported.
18*. Currency and price data are recorded.	X	¨	¨		“Costs are in 2019 GBP”.
19*. Details of currency of price adjustments for inflation or currency conversion are given.	X	¨	¨		Cost sources are not explicitly reported in the written submission. All derived from MTG49 (Rezum) – previously undergone EAC review and accepted by MTAC in 2019.
20. Details of any model used are given.	X	¨	¨	¨	Cost-minimisation analysis used.

Item	Judgement				EAC comment
	Yes	No	Not clear	Not appropriate	
21. The choice of model used and the key parameters on which it is based are justified.	¨	¨	X	¨	Some parameters are specified, assumptions have been taken from a previous model and are not all applicable or have not been consistently applied.
Analysis and interpretation of results					
22*. Time horizon of costs and benefits is stated.	X	¨	¨	¨	"A time horizon of 4 years and a cycle length of 3 months was chosen based on the availability of clinical data at the time of adapting the model (2020). Patients enter the model having undergone a surgical procedure before transitioning to one of two health states, defined by whether patients suffer from incontinence. Surgery and repeat surgery are tunnel health states, with such that, states in which patients remain for one model cycle." Model diagram is provided to demonstrate transition and Markov states. The EAC asked the Company for clarification regarding the time horizon as outcomes reported at 5 years despite the model and methods defining a time horizon of 4 years; the Company confirmed this as an error and outcomes reported are reflective of 4 years (EAC Correspondence Log, 2022).
23. The discount rate(s) is stated.	X	¨	¨	¨	"Future costs are discounted at 3.5%".
24. The choice of discount rate(s) is justified.	¨	¨	X	¨	Justification not explicitly stated, however assumed appropriate according to NICE guidance.
25. An explanation is given if costs and benefits are not discounted.	¨	¨	¨	X	N/A
26. Details of statistical tests and confidence intervals are given for stochastic data.	¨	¨	¨	X	Only difference between arms reported. No statistical tests applied.
27. The approach to sensitivity analysis is given.	X	¨	¨	¨	"Separate deterministic sensitivity analyses (DSAs) were conducted for each comparator. All primary inputs were varied in the DSA within a 20% range of the base-case value." Primary inputs used for modelling in high-risk patients derived from unpublished systematic

Item	Judgement				EAC comment
	Yes	No	Not clear	Not appropriate	
					review submitted by the Company with primary sources not explicitly reported.
28. The choice of variables for sensitivity analysis is justified.	¨	¨	X	¨	"Separate deterministic sensitivity analyses (DSAs) were conducted for each comparator. All primary inputs were varied in the DSA within a 20% range of the base-case value. Variables excluded from the sensitivity analysis included micro-costing inputs used to estimate the bundled equipment costs, the bundled adverse event costs, and pre- and post-operative costs". Justification for 20% range not explicitly reported. The Company did not include evaluation of erectile dysfunction (ED) within the original model; when this approach was queried by the EAC, the Company resubmitted an updated model and submission to incorporate ED within scenario analysis. The justification for not including this within the base case was due to the intervention (GreenLight) and comparators (HoLEP, TURP) being invasive treatment options, and "not a relevant risk factor or may not have cost implications for all men". The EAC consider this approach to be justified, however the Company do not use any inputs relating to the intervention, rather assume that outcomes for HoLEP and GreenLight are the same as two other treatment options (Transurethral needle ablation and Transurethral microwave thermotherapy) without explicit rationale. The EAC note that values within the scenario analysis are derived from a single source (Miner *et al.* 2006), which does not include GreenLight as an intervention and was published prior to GreenLight 180 W XPS being available. The EAC would consider this scenario analysis as not robust.
29. The ranges over which the variables are varied are justified.	¨	¨	X	¨	Primary inputs were varied within 20% range of the base-case value; reason for this was not explicitly reported. Uncertainty around the parameters that were updated for high-risk patients was explored using "a pseudo 95% confidence interval was derived, bounded by the low mean and the high mean. Probabilities were sampled from a beta distribution and length of stay was sampled from a log normal distribution". Authors note that the main weakness

Item	Judgement				EAC comment
	Yes	No	Not clear	Not appropriate	
					of the analysis is that there is considerable uncertainty in the some of the updated model parameters, where mid-points from high and low means reported in the Company submitted unpublished systematic review where the means were not pooled to conduct meta-analysis because of study heterogeneity. Primary sources of inputs were also not reported within the unpublished systematic review to enable replication or verification. Within non-high risk group, errors in previous PSA for Rezum were identified and described within Appendix E of the Assessment report. PSA distributions were updated in the GreenLight model for TURP and HoLEP, but not GreenLight. This was queried with the Company on several occasions; no response.
30. Relevant alternatives are compared.	X	¨	¨	¨	TURP and HoLEP are used as comparators in line with final scope (NICE, 2021).
31. Incremental analysis is reported.	¨	¨	¨	¨	Univariate analysis reported in tornado diagrams, PSA illustrated in cost effectiveness acceptability curves (Figs 3-6).
32*. Major outcomes are presented in a disaggregated as well as aggregated form.	X	¨	¨		Table 5, total cost per procedure with comparison of costs including separate reporting of costs associated with device, theatre, hospital stay, pre and post tests, treatment of short-term adverse events and incontinence, repeat surgery and short term complications, treatment of incontinence with surgery.
33*. The answer to the study question is given.	X	¨	¨		“After 5 years, the average cost per patient treated with GreenLight is £3,173 compared to £4,708 for TURP and £3,948 for HoLEP. GreenLight is estimated to result in cost-savings of £1,535 per high-risk patient treated with TURP and £776 per patient treated with HoLEP.” The EAC asked the Company for clarification regarding the time horizon as outcomes reported at 5 years despite the model and methods defining a time horizon of 4 years; the Company confirmed this as an error and outcomes reported are reflective of 4 years (EAC Correspondence Log, 2022).

Item	Judgement				EAC comment
	Yes	No	Not clear	Not appropriate	
34*. Conclusions follow from the data reported.	X	¨	¨		"This preliminary analysis suggests that it is highly likely that treating high-risk patients referred for BPH surgery with Greenlight is a cost-saving strategy compared to other surgical options offered to high-risk patients in the National Health Service (NHS)."
35*. Conclusions are accompanied by the appropriate caveats.	X	¨	¨		Limitations and weaknesses discussed in conclusions. "The weakness of this analysis is that there is considerable uncertainty in the some of the updated model parameters, where mid-points from high and low means reported in Burtt *et al.* (submitted) were selected. Burtt *et al.* (submitted) did not pool the means to conduct meta-analysis because of study heterogeneity. The uncertainty around the choice to select a mid-point was explored in scenario analyses. The EAC note that the primary sources of inputs were also not reported within the unpublished systematic review to enable replication or verification to explore the level of uncertainty within the model parameters. Methods to determine study heterogeneity was not explicitly reported.

* *"Not appropriate"* is not considered an available option

Appendix E3: PSA parameters used in GreenLight model adaptation compared to original Rezum model

PSA parameters (GreenLight Model adaptation High Risk Scenario UK 20211222 FINAL Updated 20220330)
Settings: All patients, Switch off ED
Parameters obtained from: the Sensitivity worksheet – multiple internal tabs
Key: Green highlight same as Rezum, Red highlight different to Rezum, red text value from Rezum

Sheet	Cell	Input	Therapy	Live	DSA	PSA	Distrib.	DSA Lower	DSA Upper	CI-	CI+	SE	n	Alpha	Beta	Source
Clinical	N67	Duration of operation (mins)	Mono-TURP	66.0	66.0	62.7	Log Normal	52.8	79.2	33.0	99.0					NICE MTG26 / Ray *et al.* 2016
Clinical	P67	Duration of operation (mins)	Bi-TURP	66.0	66.0	81.5	Log Normal	52.8	79.2	33.0	99.0					NICE MTG26 / Ray *et al.* 2016
Clinical	L67	Duration of operation (mins)	GreenLight	49.6	49.6	60.4	Log Normal	39.7	59.5			1.890	133			Bachmann *et al.* 2013 (GOLIATH)
Clinical	R67	Duration of operation (mins)	HoLEP	80.2	80.2	84.3	Log Normal	64.2	96.2	40.1	120.3					Lin et al 2014
Clinical	N69	Length of stay (days)	Mono-TURP	3.0	3.0	2.8	Log Normal	2.4	3.6	1.5	4.5					NICE MTG26
Clinical	P69	Length of stay (days)	Bi-TURP	2.3	2.3	2.9	Log Normal	1.9	2.8	1.2	3.5					NICE MTG26
Clinical	L69	Length of stay (days)	GreenLight	0.7	0.7	0.7	Log Normal	0.6	0.8	0.4 [0.5]	1.1 [0.8]					Ajib 2018
Clinical	R69	Length of stay (days)	HoLEP	2.0	2.0	1.4	Log Normal	1.6	2.4	1.0	3.0					NICE MTG26
Clinical	N11	Proportion required re-treatment at follow-up	Mono-TURP	0.058	0.058	0.058	Beta	0.046	0.070	0.000 [NR]	0.250 [NR]	0.064 [NR]	23,123	1,341	21,782	Madersbacher *et al.* 2006, cited Lourenco et al 2008
Clinical	P11	Proportion required re-treatment at follow-up	Bi-TURP	0.058	0.058	0.057	Beta	0.046	0.070	0.029 [NR]	0.045 [NR]	0.004 [NR]	23,123	1,341	21,782	Madersbacher *et al.* 2006, cited Lourenco et al 2008
Clinical	L11	Proportion required re-treatment at follow-up	GreenLight	0.069	0.069	0.070	Beta	0.055	0.083	0.000 [NR]	0.119 [NR]	0.030 [NR]	23,123	1,595	21,528	MTG 49, Thomas et al 2016 (GOLIATH)
Clinical	L21	Proportion retreated with TURP	GreenLight	0.500	0.500	0.479	Uniform									Assumption; 'Informed by assumptions provided by clinical experts consulted during model development'
Clinical	N29	Non-acute urinary retention	Mono-TURP	0.012	0.012	0.013	Beta	0.009	0.014	0.042 [NR]	0.160 [NR]	0.002		25	2,115.97	Lourenco *et al.* 2008; Bachmann *et al.* 2013 (GOLIATH)
Clinical	P29	Non-acute urinary retention	Bi-TURP	0.020	1.710	1.390	?NAME [Log Normal]	1.368	2.052	0.240	12.380	0.000 [NR]	0 [NR]	0 [NR]	0 [NR]	Lourenco *et al.* 2008; Bachmann *et al.* 2013 (GOLIATH)
Clinical	L29	Non-acute urinary retention	GreenLight	0.059	0.059	0.049	Beta	0.047	0.071	0.000 [NR]	0.108 [NR]	0.000 [NR]	136	8	128	Bachmann *et al.* 2013 (GOLIATH)
Clinical	R29	Non-acute urinary retention	HoLEP	0.710 [0.008]	0.710	0.934	?NAME [Log Normal]	0.568	0.852	0.006 [0.380]	0.202 [1.320]	0.000 [NR]	88 [NR]	62 [NR]	26 [NR]	Lourenco *et al.* 2008

Clinical	N31	Non-serious urinary tract infection	Mono-TURP	0.054	0.054	0.071	Beta	0.043	0.065			0.018		8 [8.5]	148 [148.2]	Lourenco *et al.* 2008
Clinical	P31	Non-serious urinary tract infection	Bi-TURP	0.054	0.054	0.071	Beta	0.043	0.065							Lourenco *et al.* 2008
Clinical	L31	Non-serious urinary tract infection	GreenLight	0.191	0.191	0.178	Beta	0.153	0.229				136	26	110	Bachmann *et al.* 2013 (GOLIATH)
Clinical	R31	Non-serious urinary tract infection	HoLEP	0.053	0.980	0.884	Log Normal	0.784	1.176	0.310	3.090					Lourenco *et al.* 2008
Clinical	L33	Bleeding (non-acute)	GreenLight	0.088	0.088	0.144	Beta	0.071	0.106				136	12	124	Bachmann *et al.* 2013 (GOLIATH)
Clinical	N41	Acute urinary retention	Mono-TURP	0.038	0.038	0.043	Beta	0.031	0.046			0.008		24	600	Lourenco *et al.* 2008
Clinical	P41	Acute urinary retention	Bi-TURP	0.066	1.710	1.682	Log Normal	1.368	2.052	0.240	12.380					Lourenco *et al.* 2008; Bachmann *et al.* 2013
Clinical	L41	Acute urinary retention	GreenLight	0.066	0.066	0.059	Beta	0.053	0.079				136	9	127	Bachmann *et al.* 2013 (GOLIATH)
Clinical	R41	Acute urinary retention	HoLEP	0.027	0.710	0.792	Log Normal	0.568	0.852	0.380	1.320					Lourenco *et al.* 2008
Clinical	N43	Bladder neck contracture / stricture	Mono-TURP	0.070	0.070	0.066	Beta	0.056	0.084	0.041 [NR]	0.101 [NR]	0.010	NR [NR]	46 [45.5]	604.50	Lourenco *et al.* 2008
Clinical	P43	Bladder neck contracture / stricture	Bi-TURP	0.070 [0.097]	1.000 [1.380]	1.608	#NAME? [Log Normal]	0.800 [1.104]	1.200 [1.656]	0.450	4.260	0.972 [NR]	- [NR]	- 1 [NR]	- [NR]	Lourenco *et al.* 2008
Clinical	L43	Bladder neck contracture / stricture	GreenLight	0.044	0.044	0.021	Beta	0.035	0.053	0.000 [NR]	0.006 [NR]	0.002 [NR]	136	6	130	Bachmann *et al.* 2013 (GOLIATH)
Clinical	R43	Bladder neck contracture / stricture	HoLEP	0.070 [0.059]	1.000 [0.840]	0.747	#NAME? [Log Normal]	0.800 [0.672]	1.200 [1.008]	0.430	1.650	0.311 [NR]		- 1 [NR]	- [NR]	Lourenco *et al.* 2008
Clinical	N45	Bleeding / Blood transfusion	Mono-TURP	0.080	0.080	0.123	Beta	0.064	0.096	0.000 [NR]	0.223 [NR]	0.020 [NR]		15 [14.6]	168.36 [168.4]	Lourenco *et al.* 2008
Clinical	P45	Bleeding / Blood transfusion	Bi-TURP	0.080 [0.082]	1.000 [1.030]	1.347	#NAME? [Log Normal]	0.800 [0.824]	1.200 [1.000]	0.430 [0.240]	1.650 [4.490]	0.311 [NR]	- [NR]	- 1 [NR]	- [NR]	Lourenco *et al.* 2008
Clinical	L45	Bleeding / Blood transfusion	GreenLight	0.029	0.029	0.022	Beta	0.024	0.035	0.009 [NR]	0.190 [NR]	0.046 [NR]	136	4	132	Bachmann *et al.* 2013 (GOLIATH)
Clinical	R45	Bleeding / Blood transfusion	HoLEP	0.080 [0.022]	1.000 [0.270]	#NUM!	#NAME? [Log Normal]	0.800 [0.216]	1.200 [0.324]	0.430 [0.070]	0.395 [0.950]	-0.009 [NR]	- [NR]	- 1 [NR]	- [NR]	Lourenco *et al.* 2008
Clinical	N47	Transurethral resection syndrome	Mono-TURP	0.030	0.030	0.027	Beta	0.024	0.036			0.010		8.7	281.3	Lourenco *et al.* 2008
Clinical	P47	Transurethral resection syndrome	Bi-TURP	0.005	0.180	0.155	Log Normal	0.144	0.216	0.050	0.620					NICE, MTG23
Clinical	R47	Transurethral resection syndrome	HoLEP	0.009	0.310	0.098	Log Normal	0.248	0.372	0.010	7.390					Lourenco *et al.* 2008
Clinical	N49	Urinary tract infection	Mono-TURP	0.006	0.006	0.008	Beta	0.005	0.007			0.002		8.9	1,481.1	Lourenco *et al.* 2008
Clinical	P49	Urinary tract infection	Bi-TURP	0.006	1.000	0.181	Log Normal	0.800	1.200	0.070	15.120					Lourenco *et al.* 2008
Clinical	R49	Urinary tract infection	HoLEP	0.006	0.980	0.791	Log Normal	0.784	1.176	0.310	3.090					Lourenco *et al.* 2008
Clinical	N57	Incontinence	Mono-TURP	0.030	0.030	0.030	Beta	0.024	0.036			0.008 [0.010]		15.5 [8.7]	500.8 [281.3]	Lourenco *et al.* 2008
Clinical	P57	Incontinence	Bi-TURP	0.018	0.590	0.925	Log Normal	0.472	0.708	0.080	4.310					Lourenco *et al.* 2008
Clinical	L57	Incontinence	GreenLight	0.011	0.011	0.022	Beta	0.009	0.013				136	1	135	Bachmann *et al.* 2013 (GOLIATH)
Clinical	R57	Incontinence	HoLEP	0.029	0.970	1.102	Log Normal	0.776	1.164	0.530	1.270					Lourenco *et al.* 2008
Costs	N11	Bundled cost	Mono-TURP	165.3 [119.984]	165.3	163.6	Gamma	132.3	198.4			16.535		100	2 [1]	See detailed breakdown

Costs	P11	Bundled cost	Bi-TURP	255.7 [210.238]	255.7	223.4	Gamma	204.6	306.9			25.572		100	3 [2]	See detailed breakdown
Costs	L11	Bundled cost	GreenLight	550.0 [540]	550.0 [540]	579.8	Gamma	440.0	660.0			55.000		100	6 [15]	See detailed breakdown
Costs	R11	Bundled cost	HoLEP	448.8	448.8	408.5	Gamma	359.1	538.6			44.883		100	4 [5]	See detailed breakdown
Costs	L17	Cost of operating theatre (per min)	All	13.4 [13.37]	13.37	13.117	Gamma	10.696	16.044			1.337		100	0	See detailed breakdown
Costs	L21	Cost of hospital bed-day	All	365.0	365.00	380.656	Gamma	292.000	438.000			36.500		100	4	See detailed breakdown
Costs	L35	Pre-operative tests	All	129.2	129.20	140.909	Gamma	103.360	155.040			12.920		100	1	See detailed breakdown
Costs	L37	Post-operative tests	All	129.2	129.20	155.956	Gamma	103.360	155.040			12.920		100	1	See detailed breakdown
Costs	L27	Pre-operative Urologist consultation	All	127.0	127.00	109.972	Gamma	101.600	152.400			12.700		100	1	See detailed breakdown
Costs	L29	Post-operative Urologist consultation	All	105.0	105.00	97.004	Gamma	84.000	126.000			10.500		100	1	NHS reference costs 2017/2018

Abbreviations: HoLEP, holmium laser enucleation of the prostate; bi-TURP, bipolar transurethral resection of the prostate; mono-TURP, monopolar transurethral resection of the prostate; mins, minutes; NR, not reported.

Appendix E4: EAC model replication and basecase using rdecision

Rezum/Greenlight Markov model

Andrew Sims, Kim Keltie

20/04/2022

Model

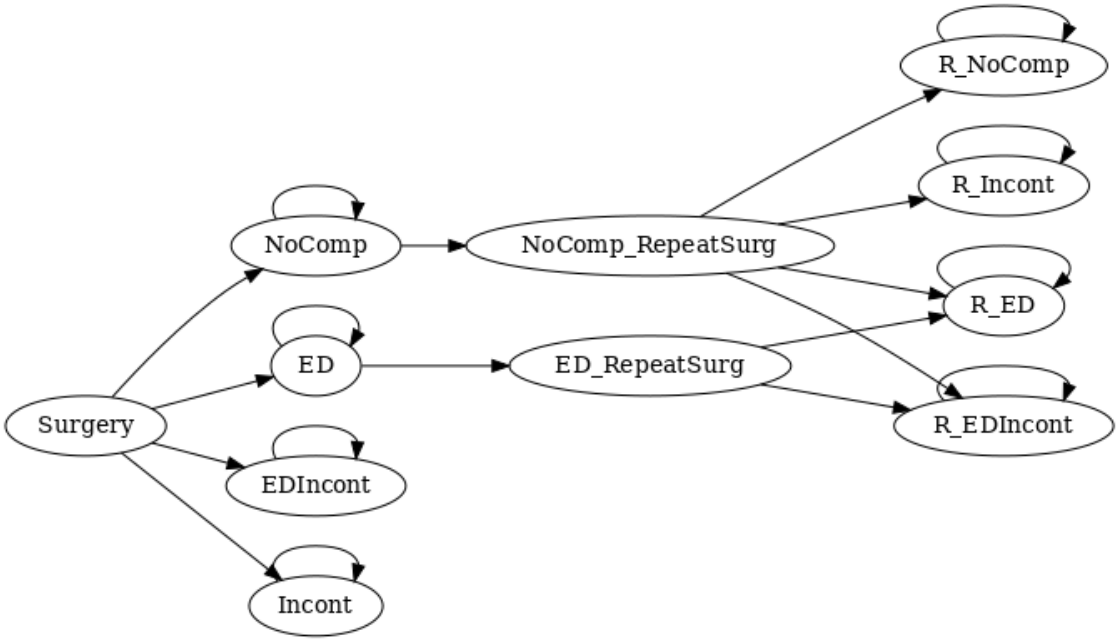
Model structure

The company developed a model in Excel for MTG49 (Rezum) and modified it for the GreenLight guidance review. The EAC replicated the company's original model for Rezum in R, using the `rdecision` package (from CRAN), and modified it for additional scenarios.

The approach is a semi Markov model with 11 states. Three states represent an interventional procedure: "Surgery" (the initial procedure), "NoComp_RepeatSurg" (surgical retreatment) not associated with resolving erectile dysfunction, and "ED_RepeatSurg", surgical retreatment associated with resolving erectile dysfunction. Implicitly, a proportion of the surgical retreatments are assumed to be with TURP. The three interventional procedure states are temporary states occupied for one cycle (fixed at 0.25 years).

It is a "semi" Markov model because the transitions are defined as probabilities (of starting a cycle in one state and ending the cycle in another), rather than as instantaneous rates. The company derived transition probabilities (p) from rates (r), using the relationship $p = 1 - \exp(-rt)$. The EAC notes that although this is a common approach, the formula is true only for a two-state, one transition, model and is only an approximation for more complex models, because it assumes that a patient can make no more than one transition per cycle. Further explanation is provided in R package *rdecision* and references therein.

The model is non-comparative; that is, a single instance models the costs of a single type of procedure and its associated longer-term consequences. Different scenarios are modelled by running an instance of the model using a set of model variables applicable to the scenario, including the procedure cost.


R_NoComp
R_Incont
NoComp
NoComp_RepeatSurg
R_ED
ED
ED_RepeatSurg
Surgery
R_EDIncont
EDIncont
Incont

Model variables

The model uses 14 variables associated with the scope that are not specific to the type of intervention. These are as follows (all costs in GBP):

Name	Description
c_PrePost	Cost of pre- and post procedure tests
c_theatre	Theatre costs (per minute)
c_LoS	Cost per day of hospital stay
p_MonoBi	Proportion of surgical retreatments with TURP using monopolar TURP
c_UrReten_NS	Cost of treating short-term, non-severe urinary retention
c_Bleeding_NS	Cost of treating short-term, non-severe bleeding
c_UTI_NS	Cost of treating short-term, non-severe UTI
c_UrReten_S	Cost of treating short-term, severe urinary retention
c_BladderStricture_S	Cost of treating short-term, severe bladder neck contracture
c_Bleeding_S	Cost of treating short-term, severe bleeding
c_TURS_S	Cost of treating short-term severe TUR syndrome
c_UTI_S	Cost of treating short term, severe UTI
c_incontinence	Cost of managing long-term urinary incontinence
c_ED	Cost of treating long-term erectile dysfunction

It uses a further 16 variables whose value depends on the type of intervention. These are as follows (all costs in GBP):

Name	Description
c_device	Cost of the technology
t_theatre	Duration of surgery (minutes)
t_LoS	Length of stay (days)
p_retreat	Reported proportion requiring surgical retreatment
t_FU	Reported follow-up time for p_retreat (years)
p_retreat_TURP	Proportion retreated with TURP
p_UrReten_NS	Proportion with short-term, non-severe urinary retention
p_UTI_NS	Proportion with short-term, non-severe UTI
p_Bleeding_NS	Proportion with short-term non-severe bleeding
p_UrReten_S	Proportion with short-term, severe urinary retention
p_BladderStricture_S	Proportion with short-term, severe bladder neck contracture
p_Bleeding_S	Proportion with short-term, severe bleeding
p_TURS_S	Proportion with short-term, severe TUR syndrome

Name	Description
p_UTI_S	Proportion with short-term, severe UTI
p_Incontinence	Proportion with long-term urinary incontinence
p_ED	Proportion with long-term erectile dysfunction

Results

MTG49 (Rezum)

The EAC replicated the company base case presented for the assessment of the Rezum procedure, for MTG49. It is presented here for verification of the EAC model structure and inputs, and replicates the results presented by the EAC's replication of the company's model for MTG49 (see Appendix E of the EAC Report for Rezum, October 2019).

The values of the common model variables were as follows:

Description	Value
Cost of pre- and post procedure tests	490.4
Theatre costs (per minute)	13.37
Cost per day of hospital stay	370.3
Proportion of surgical retreatments with TURP using monopolar TURP	0.5
Cost of treating short-term, non-severe urinary retention	40.61
Cost of treating short-term, non-severe bleeding	38.29
Cost of treating short-term, non-severe UTI	39.18
Cost of treating short-term, severe urinary retention	3062
Cost of treating short-term, severe bladder neck contracture	330
Cost of treating short-term, severe bleeding	357.9
Cost of treating short-term severe TUR syndrome	2102
Cost of treating short term, severe UTI	781
Cost of managing long-term urinary incontinence	2357
Cost of treating long-term erectile dysfunction	198.8

The values of the intervention-specific variables were as follows:

Description	Rezum	monoTURP	biTURP	UroLift	GreenLight	HoLEP
Cost of the technology	1348	120.01	210.38	1559.45	550	448.83
Duration of surgery (minutes)	17.5	66	66	30	49.6	80.19
Length of stay (days)	0.5	3.03	2.33	0.5	0.7	1.98

Description	Rezum	monoTURP	biTURP	UroLift	GreenLight	HoLEP
Reported proportion requiring surgical retreatment	0.044	0.058	0.058	0.136	0.058	0
Reported follow-up time for p_retreat (years)	4	5	5	5	5	5.2
Proportion retreated with TURP	0.5	1	1	1	0.5	0
Proportion with short-term, non-severe urinary retention	0.02645	0.01153	0.01973	0.01428	0.05882	0.00819
Proportion with short-term, non-severe UTI	0.02116	0.054	0.054	0.02857	0.19117	0.05292
Proportion with short-term non-severe bleeding	0	0	0	0	0.08823	0
Proportion with short-term, severe urinary retention	0.00529	0.03846	0.06576	0	0.06617	0.0273
Proportion with short-term, severe bladder neck contracture	0.01058	0.07	0.0966	0	0.04411	0.0588
Proportion with short-term, severe bleeding	0	0.08	0.0824	0	0.02941	0.0216
Proportion with short-term, severe TUR syndrome	0	0.03	0.0054	0	0	0.0093
Proportion with short-term, severe UTI	0	0.006	0.006	0	0	0.00588
Proportion with long-term urinary incontinence	0	0.03	0.0177	0	0.011	0.0291
Proportion with long-term erectile dysfunction	0	0.1	0.1	0	0.02	0.02

The time horizon was 4 years. The costs for each interventional procedure type, without and with considering erectile dysfunction as an adverse event, were as follows. The final two columns give the costs relative to Rezum (negative means Rezum is cost saving). The values were within 0.1% of the company's *de novo* base case submission for Rezum.

Intervention	NoED	ED	NoED.Rel	ED.Rel
Rezum	2378.01	2378.67	0	0
UroLift	2915.99	2919.32	-537.98	-540.66

Intervention	NoED	ED	NoED.Rel	ED.Rel
GreenLight	2403.33	2418.87	-25.32	-40.2
HoLEP	3137.08	3151.88	-759.07	-773.21
monoTURP	3235.07	3309.58	-857.06	-930.91
biTURP	2994.62	3069.33	-616.61	-690.66
TURP	3114.84	3189.45	-736.83	-810.78

Company Markov model for Greenlight

The company model for GreenLight, which included all patients, was based on the original model Markov model submitted for Rezum (MTG49, 2019), with some modifications to the model variables. The values of the common model variables were as follows:

Description	Value
Cost of pre- and post procedure tests	490.4
Theatre costs (per minute)	13.37
Cost per day of hospital stay	365
Proportion of surgical retreatments with TURP using monopolar TURP	0.5
Cost of treating short-term, non-severe urinary retention	40.61
Cost of treating short-term, non-severe bleeding	38.29
Cost of treating short-term, non-severe UTI	39.18
Cost of treating short-term, severe urinary retention	3062
Cost of treating short-term, severe bladder neck contracture	330
Cost of treating short-term, severe bleeding	357.9
Cost of treating short-term severe TUR syndrome	2102
Cost of treating short term, severe UTI	781
Cost of managing long-term urinary incontinence	2280
Cost of treating long-term erectile dysfunction	198.8

The values of the intervention-specific variables were as follows:

Description	monoTURP	biTURP	GreenLight	HoLEP
Cost of the technology	165.35	255.72	550	448.83
Duration of surgery (minutes)	66	66	49.6	80.2
Length of stay (days)	3.03	2.33	0.7	2
Reported proportion requiring surgical retreatment	0.058	0.058	0.069	0
Reported follow-up time for p_retreat (years)	5	5	5	5.2
Proportion retreated with TURP	1	1	0.5	0

Description	monoTURP	biTURP	GreenLight	HoLEP
Proportion with short-term, non-severe urinary retention	0.012	0.02	0.059	0.008
Proportion with short-term, non-severe UTI	0.054	0.054	0.191	0.053
Proportion with short-term non-severe bleeding	0	0	0.088	0
Proportion with short-term, severe urinary retention	0.038	0.066	0.066	0.027
Proportion with short-term, severe bladder neck contracture	0.07	0.097	0.044	0.059
Proportion with short-term, severe bleeding	0.08	0.082	0.029	0.022
Proportion with short-term, severe TUR syndrome	0.03	0.005	0	0.009
Proportion with short-term, severe UTI	0.006	0.006	0	0.006
Proportion with long-term urinary incontinence	0.03	0.018	0.011	0.029
Proportion with long-term erectile dysfunction	0.08	0.08	0.01	0.01

The time horizon was 4 years. The costs for each interventional procedure type, were as follows. The final two columns give the costs relative to GreenLight (negative means GreenLight is cost saving).

Intervention	NoED	NoED.Rel
GreenLight	2416.01	0
HoLEP	3123.54	-707.53
monoTURP	3255.24	-839.22
biTURP	3026.15	-610.14
TURP	3140.69	-724.68

Company "high risk" model for GreenLight

The company proposed modifications to the base case to represent a high risk group of patients. The changes are listed in Table 23.

The values of the common model variables were as follows:

Description	Value
Cost of pre- and post procedure tests	490.4
Theatre costs (per minute)	13.37
Cost per day of hospital stay	370.3
Proportion of surgical retreatments with TURP using monopolar TURP	0.5
Cost of treating short-term, non-severe urinary retention	40.61
Cost of treating short-term, non-severe bleeding	38.29
Cost of treating short-term, non-severe UTI	39.18

Description	Value
Cost of treating short-term, severe urinary retention	3062
Cost of treating short-term, severe bladder neck contracture	330
Cost of treating short-term, severe bleeding	357.9
Cost of treating short-term severe TUR syndrome	2102
Cost of treating short term, severe UTI	781
Cost of managing long-term urinary incontinence	2357
Cost of treating long-term erectile dysfunction	198.8

The values of the intervention-specific variables were as follows:

Description	monoTURP	biTURP	GreenLight	HoLEP
Cost of the technology	165.35	255.72	550	448.83
Duration of surgery (minutes)	66	66	49.6	80.19
Length of stay (days)	6.85	6.8	2.95	3.15
Reported proportion requiring surgical retreatment	0.125	0.037	0.0595	0.146
Reported follow-up time for p_retreat (years)	5	5	5	5.2
Proportion retreated with TURP	1	1	0.5	0
Proportion with short-term, non-severe urinary retention	0.0075	0.0075	0.0835	0.104
Proportion with short-term, non-severe UTI	0.054	0.054	0.19117	0.05292
Proportion with short-term non-severe bleeding	0	0	0.08823	0
Proportion with short-term, severe urinary retention	0.03846	0.06576	0.032	0.0273
Proportion with short-term, severe bladder neck contracture	0.071	0.0715	0.0045	0.045
Proportion with short-term, severe bleeding	0.1115	0.2095	0.1545	0.1975
Proportion with short-term, severe TUR syndrome	0.03	0.0054	0	0.0093
Proportion with short-term, severe UTI	0.006	0.006	0	0.00588
Proportion with long-term urinary incontinence	0.03	0.0177	0.011	0.0291
Proportion with long-term erectile dysfunction	0.1	0.1	0.02	0.02

The time horizon was 4 years. The costs for each interventional procedure type, were as follows. The final two columns give the costs relative to GreenLight (negative means GreenLight is cost saving).

Intervention	NoED	NoED.Rel
GreenLight	3216.06	0
HoLEP	3971.35	-755.29
monoTURP	4970.53	-1754.47
biTURP	4735.44	-1519.38
TURP	4852.99	-1636.92

EAC base case for GreenLight

The EAC base case for Greenlight is per MTG49 (Rezum) base case, with the following changes:

- Cost of Greenlight: 540 GBP;
- Cost of HoLEP is 450.63 GBP. This is an increase of 1.80 GBP due to the previous misapplication of 1 a year discount to the capital costs (51.44 GBP at 3.5%).
- Cost of monoTURP is 165.35 GBP (adds saline irrigation costs of 45.34 GBP to MTG49 costs);
- Cost of biTURP is 255.72 GBP (adds saline irrigation costs of 45.24 GBP to MTG49 costs);
- LoS for GreenLight and HoLEP are 1.6 days;
- LoS for monoTURP and biTURP is 2.3 days;
- Proportion of mono polar TURP is 38%;
- 0.25% of GreenLight procedures are converted to TURP. This is modelled by adding the procedure cost of TURP (which includes procedural adverse events) to 0.25% of GreenLight cases. The model structure does not permit including longer-term consequences of cases converted to TURP.
- Changing the time horizon to 5 years

Point estimate

The values of the common model variables were as follows:

Description	Value
Cost of pre- and post procedure tests	490.4
Theatre costs (per minute)	13.37
Cost per day of hospital stay	370.3
Proportion of surgical retreatments with TURP using monopolar TURP	0.38
Cost of treating short-term, non-severe urinary retention	40.61
Cost of treating short-term, non-severe bleeding	38.29
Cost of treating short-term, non-severe UTI	39.18

Description	Value
Cost of treating short-term, severe urinary retention	3062
Cost of treating short-term, severe bladder neck contracture	330
Cost of treating short-term, severe bleeding	357.9
Cost of treating short-term severe TUR syndrome	2102
Cost of treating short term, severe UTI	781
Cost of managing long-term urinary incontinence	2357
Cost of treating long-term erectile dysfunction	198.8

The values of the intervention-specific variables were as follows:

Description	monoTURP	biTURP	GreenLight	HoLEP
Cost of the technology	165.35	255.72	546.78	450.63
Duration of surgery (minutes)	66	66	49.6	80.19
Length of stay (days)	2.3	2.3	1.6	1.6
Reported proportion requiring surgical retreatment	0.058	0.058	0.058	0
Reported follow-up time for p_retreat (years)	5	5	5	5.2
Proportion retreated with TURP	1	1	0.5	0
Proportion with short-term, non-severe urinary retention	0.01153	0.01973	0.05882	0.00819
Proportion with short-term, non-severe UTI	0.054	0.054	0.19117	0.05292
Proportion with short-term non-severe bleeding	0	0	0.08823	0
Proportion with short-term, severe urinary retention	0.03846	0.06576	0.06617	0.0273
Proportion with short-term, severe bladder neck contracture	0.07	0.0966	0.04411	0.0588
Proportion with short-term, severe bleeding	0.08	0.0824	0.02941	0.0216
Proportion with short-term, severe TUR syndrome	0.03	0.0054	0	0.0093
Proportion with short-term, severe UTI	0.006	0.006	0	0.00588
Proportion with long-term urinary incontinence	0.03	0.0177	0.011	0.0291
Proportion with long-term erectile dysfunction	0.1	0.1	0.02	0.02

The time horizon was 5 years. The costs for each interventional procedure type, were as follows. The final two columns give the costs relative to GreenLight (negative means GreenLight is cost saving).

Intervention	NoED	NoED.Rel
GreenLight	2787.14	0
HoLEP	3056.66	-269.52
monoTURP	3089.05	-301.9
biTURP	3093.76	-306.62
TURP	3091.97	-304.83

Probabilistic sensitivity analysis

The EAC conducted a PSA around its base case (without ED adverse effects) using a restricted number of parameters considered to be uncertain. These were as follows:

- Proportion undergoing monopolar TURP (from BAUS BOO audit, 2019); 332 cases of monopolar TURP and 548 cases of bipolar TURP (Beta distribution, α = 332, β = 548);
- Procedure duration. Hyperparameters were based on Rezum company submission by fitting to the confidence intervals using the method of moments. However, the confidence intervals in Table 11 of the company submission for theatre time seem implausibly wide (e.g. HoLEP 40.1 mins to 120.3 mins) because the confidence intervals are supposed to represent uncertainty in the estimate of mean theatre time, *not* the centiles of the distribution of operating times themselves.

The distributions of the variables included in the PSA were as follows:

Variable	Unit	Distribution	Mean	P2.5	P97.5
mTURP proportion		Be(332,548)	0.3773	0.3455	0.4095
Theatre time, HoLEP	min	LN(4.345,0.28)	80.19	44.51	133.5
Theatre time, mTURP	min	LN(4.15,0.28)	66	36.64	109.9
Theatre time, biTURP	min	LN(4.15,0.28)	66	36.64	109.9
Theatre time, GreenLight	min	LN(3.816,0.42)	49.6	19.93	103.5

From 1000 runs, the mean (95% CI) cost of each intervention, the mean (95%CI) cost relative to GreenLight (negative values mean GreenLight is cost saving), and the proportion of runs in which GreenLight is cost saving, are shown below.

Intervention	Cost (95% CI)	Difference	% saving
GreenLight	2783.72 (2389.68 to 3503.41)	-	-
HoLEP	3049.02 (2567.31 to 3799.51)	-265.30 (-1171.35 to 601.35)	75.1
monoTURP	3086.09 (2661.84 to 3702.35)	-302.37 (-1068.79 to 531.63)	80.3
biTURP	3099.90 (2689.09 to 3716.87)	-316.19 (-1033.04 to 525.40)	82.1

Intervention	Cost (95% CI)	Difference	% saving
TURP	3094.85 (2783.51 to 3531.36)	-311.13 (-894.41 to 487.18)	83.1

Univariate threshold analysis

The theatre time and length of stay for TURP and for HoLEP were changed univariately to find the threshold at which those technologies would become cost saving with respect to GreenLight. This acknowledges the uncertanties in these parameters for the competing technologies. The thresholds are as follows:

Variable	Value	Unit
Theatre time, TURP	43.74	min
Theatre time, HoLEP	60.03	min
LoS, TURP	1.496	day
LoS, HoLEP	0.8722	day

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology guidance scope

Greenlight XPS for treating benign prostatic hyperplasia

1 Technology

1.1 Description of the technology

The GreenLight XPS (Boston Scientific) is intended for laser vaporisation of the prostate in the treatment of benign prostatic hyperplasia (BPH). The GreenLight procedure, known as photoselective vaporisation of prostatic tissue, is performed by inserting a laser cystoscope with a camera system trans-urethrally. During the procedure a laser fibre is passed through a cystoscope to vaporise the enlarged prostate, leaving a clear urethral channel. If bleeding occurs, Greenlight XPS can utilise its 'coagulation' mode, which uses a pulsating laser light to seal (cauterise) any bleeding vessels that may result from photoselective vaporisation. The GreenLight XPS laser operates at a shorter wavelength (532 nanometres) than other laser systems used to treat BPH. The shorter wavelength light is absorbed by oxyhaemoglobin (in blood and tissue), which vaporises the tissue, leaving no fragments behind. GreenLight XPS uses a proprietary MoXy laser fibre, which is actively cooled using a flow of saline to minimise degradation and improve fibre durability.

The GreenLight console and its associated fibres have been developed and upgraded since its first introduction in 2005. The latest version of Greenlight XPS uses a 180w, 532nm wavelength laser. This system is designed to allow the use of 1 fibre per patient in all but the largest prostate.

The procedure can be done either as day-case or inpatient treatment. The system requires training, and a mentoring scheme is in place with the NHS for urological surgeons to carry this out.

1.2 Relevant diseases and conditions

Greenlight XPS is indicated for the treatment of benign prostatic hyperplasia (BPH). BPH is the most common cause of lower urinary tract symptoms (LUTS). Growth of the prostate causes outflow obstruction and surgical treatments seek to improve symptoms secondary to BPH by removing excess prostate tissue. LUTS can be categorised into voiding, storage and post-micturition symptoms. Voiding symptoms are the most common and include: weak or intermittent urinary stream; straining; hesitancy; terminal dribbling and incomplete emptying. However, storage symptoms are more bothersome and include: urgency; frequency; urgency incontinence and nocturia. Mixed symptoms (both storage and voiding) are common in patients with bladder outflow obstruction (BOO) secondary to BPH. Increasingly severe LUTS are also associated with a rising prevalence of erectile and ejaculatory dysfunction.

Benign prostate hyperplasia (BPH) is common in men over 50 and increases with age with the incidence of BPH estimated to increase from 50% among men between the ages of 50 and 60 years, to 90% for men older than 80 years of age (Urology Foundation). The effect of LUTS on quality of life can be assessed using the International Prostate Symptoms Score (IPSS). A score of 8-19 is classified as moderate, while 20-35 is classified as severe. Moderate-to-severe LUTS are present in about 40% of men older than 50 years of age, rising to 90% of men in their eighties (Patient UK). Moderate to severe LUTS are estimated to affect up to 3.4 million men in the UK (Rees, 2014).

1.3 Current management

Current management for men with lower urinary tract symptoms is outlined in NICE guideline Lower urinary tract symptoms (2010) and in the NICE pathway, Lower urinary tract symptoms in men overview. Mild symptoms are usually managed conservatively including containment products, lifestyle

factors and observation. Drugs such as alpha blockers and 5-alpha-reductase inhibitors may also be used. If symptoms worsen over time, or conservative management or drug treatment options are inappropriate or unsuccessful, surgical options may be discussed. There are several considerations to inform the most appropriate management options for individuals, which include the severity of symptoms, size and shape of the prostate and median lobe and any additional comorbidities.

Surgical options include monopolar or bipolar TURP, transurethral vaporisation of the prostate (TUVP) or holmium laser enucleation of the prostate (HoLEP). Transurethral incision of the prostate (TUIP) may be offered if the prostate is estimated to be smaller than 30ml. Open prostatectomy should only be offered if the prostate is estimated to be larger than 80ml. More recently, alternative surgical approaches including prostatic urethral lift (PUL), water vapour thermal therapy, transurethral resection and haemostasis of the prostate and photoselective laser vaporisation techniques have been demonstrated to be alternatives each in their own indications.

1.4 Regulatory Status

The current version of Greenlight XPS (180w) and its associated liquid cooled fibre system received CE marking class IIB in 2010. The GreenLight XPS console is a class IIB device, and the MoXy disposable laser fibre is a class IIA device. The first version of GreenLight was CE marked in 2005.

1.5 Claimed benefits

The benefits of GreenLight XPS to patients by the company are:

- Shorter hospital length of stay, because the GreenLight XPS procedure can be done as a day-case procedure
- Shorter duration of catheterisation
- Quicker return to normal activity following treatment
- Lower likelihood of rehospitalisation within 30 days post procedure

- Reduction in patient stress and anxiety because typically no overnight stay is needed
- Reduction in pain leading to improved quality of life
- May be used in patients with comorbidities; those older in age, taking anticoagulants, with larger prostates and with urinary retention.
- Reduced risk of excessive or severe bleeding, TUR syndrome
- Reduced requirement for blood transfusion.

The benefits to the healthcare system claimed by the company are:

- Procedure performed as a day case rather than as an inpatient
- Reduced length of stay in hospital
- Reduced risk of adverse events from bleeding and transurethral resection of the prostate (TURP) syndrome
- Reduction in hospital readmissions within 30 days post procedure
- Reduced requirement for blood transfusion.

2 Decision problem

Population	People with urinary outflow obstruction secondary to benign prostatic hyperplasia in whom surgical intervention is indicated, especially those with prostates that are larger than ≥30ml.
Intervention	Greenlight XPS Photoselective Vaporisation of the Prostate (PVP)
Comparator(s)	• Monopolar and bipolar transurethral resection of the prostate (TURP) • Holmium laser enucleation of the prostate (HoLEP)
Outcomes	The outcome measures to consider to be included: **Patient outcomes** • symptoms of BPH (International Prostate Symptom Score [IPSS] • change in prostate volume • maximum flow rate (Qmax) • post void residual volume (PVR) • duration of catheterisation • rate of dysuria (pain) • quality of life measures, e.g., International Prostate Symptom Score Quality of Life (IPSS-QOL) • preservation of sexual function **System outcomes** • length of hospital stay

	• frequency of completion as a day case • rate of re-admission • procedural blood loss and blood transfusion requirement **Adverse effects** • rate of transurethral resection syndrome (TUR) • rate of capsular perforation • device related adverse events
Cost analysis	Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be long enough to reflect differences in costs and consequences between the technologies being compared. Comparators: monopolar TURP, bipolar TURP and holmium laser enucleation of the prostate (HoLEP). Monopolar,and bipolar TURP should be included as in-patient procedures in the cost model to reflect the setting they are routinely used in the NHS. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers and combinations of devices are needed.

Subgroups to be considered	• **High risk patients** should be considered as a subgroup due to the different resource consequences for this population. This group may include:
	  • people with pacemakers or defibrillators and those at risk of bleeding sequelae (including people on anti-coagulation therapy, with a history of bleeding disorders, an implanted prosthetic heart valve, implanted coronary stents, patients on aspirin therapy for prior coronary events, patients with prior deep vein thrombosis [DVT] or a high risk of DVT, stroke survivors, haemophiliacs, and patients who do not wish to have blood transfusions).
	  • people with a prostate size greater than 100ml
	  • people with urinary retention
	• **Settings** of the procedure should be considered as separate groups given the cost implications from this. The procedure is expected to be carried out as a day case, but a small proportion of individuals may be admitted as inpatients.

Special considerations, including those related to equality	The condition of BPH is most common in men over the age of 50, so the GreenLight XPS laser system is primarily for use in this population. This is a function of the clinical condition for which the technology is indicated and is not likely to be considered an equalities issue. LUTS secondary to BPH are more prevalent in black men than men of white or Asian origin. This is also a function of the clinical condition, not of the technology itself. Laser vaporisation technology such as GreenLight has the potential to reduce the risk of bleeding compared with other surgical options and so may improve access to medical treatment for BPH in these previously excluded groups. These may include

	people on anticoagulant therapies, those with bleeding disorders and those whose beliefs prevent them from receiving blood transfusions, many of whom may be covered under the 2010 Equality Act. This technology may be appropriate for individuals who do not identify as male but have a prostate and may have BPH that requires treatment. Gender is a protected characteristic under the 2010 Equality Act. Greenlight is contraindicated for people with prostate cancer. Cancer is recognised as a disability. Disability is a protected characteristic under the 2010 Equality Act.	
Special considerations, specifically related to equality	Are there any people with a protected characteristic for whom this device has a particularly disadvantageous impact or for whom this device will have a disproportionate impact on daily living, compared with people without that protected characteristic?	No
	Are there any changes that need to be considered in the scope to eliminate unlawful discrimination and to promote equality?	No
	Is there anything specific that needs to be done now to ensure the Medical Technologies Advisory Committee will have relevant information to consider equality issues when developing guidance?	No
Any other special considerations	People who wish to preserve sexual function and fertility.	

3 Related NICE guidance

Published

- UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia. NICE medical technologies guidance, May 2021 [MTG58] Available here: https://www.nice.org.uk/guidance/mtg58
- The PLASMA system for transurethral resection and haemostasis of the prostate. NICE medical technologies guidance, January 2021 [MTG53] Available here: https://www.nice.org.uk/guidance/mtg53
- Rezum for treating lower urinary tract symptoms secondary to benign prostatic hyperplasia. NICE medical technologies guidance, June 2020 [MTG49]. Available here: https://www.nice.org.uk/guidance/mtg49
- Lower urinary tract symptoms in men. NICE pathway, last updated April 2020. Available from: https://pathways.nice.org.uk/pathways/lower-symptoms-in-men

- Prostatic urethral temporary implant insertion for lower urinary tract symptoms caused by benign prostatic hyperplasia. NICE interventional procedures guidance IPG641. January 2019. Available here: https://www.nice.org.uk/guidance/IPG641
- Transurethral water vapour ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia. NICE Interventional procedures guidance IPG625. August 2018. Available here: https://www.nice.org.uk/guidance/ipg625/chapter/1-Recommendations
- Prostate artery embolization for lower urinary tract symptoms caused by benign prostatic hyperplasia. NICE IPG611. April 2018. Available here: https://www.nice.org.uk/guidance/ipg611
- Memokath-028, 044 and 045 stents for urethral obstruction. NICE medtech innovation briefing MIB123, October 2017. Available from: https://www.nice.org.uk/advice/mib123
- Insertion of prostatic urethral lift implants to treat lower urinary tract symptoms secondary to benign prostatic hyperplasia. NICE IPG475. January 2014. Available here: https://www.nice.org.uk/guidance/ipg475/history
- Lower urinary tract symptoms in men: management. Clinical guideline [CG97], May 2010. Available from: https://www.nice.org.uk/Guidance/CG97

In development

NICE is developing the following guidance:

- Guidelines update to CG97: Lower urinary tract symptoms in men: management. Clinical Guideline update, publication date to be confirmed as stated here: https://www.nice.org.uk/guidance/cg97/resources/2019-surveillance-of-lower-urinary-tract-symptoms-in-men-management-nice-guideline-cg97-6965648749/chapter/Surveillance-decision?tab=evidence
- Interventional Procedure Guideline in development for prostatic urethral temporary implant insertion for lower urinary tract symptoms caused by benign prostatic hyperplasia. Publication date to be confirmed, as stated here: https://www.nice.org.uk/guidance/indevelopment/gid-ipg10214

4 External organisations

4.1 Professional

The following organisations have been asked to comment on the draft scope:

- British Association of Day Surgery
- The Royal College of Anaesthetists
- The Association of Anaesthetists
- British Association of Urological Surgeons
- The Association for Perioperative Practice
- British Prostate Group
- Royal College of Surgeons of England
- The British association of Urological Nurses (BAUN)
- Getting it right first time (GIRFT)

4.2 Patient

NICE's Public Involvement Programme contacted the following organisations for patient commentary and asked them to comment on the draft scope:

- Anticoagulation UK
- Bladder Health UK
- Bladder and Bowel UK
- Everyman
- Orchid (for penile, prostate and testicular cancer)
- Men's Health Forum (MHF)
- Prostate Cancer UK
- Prostate Help Association
- Sexual Advice Association
- Tackle prostate cancer
- The Haemophilia Society
- The Urology Foundation

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology guidance

Guidance update assessment report overview

GID-MT564 GreenLight XPS for treating benign prostatic hyperplasia

An update of MTG29

This assessment report update overview has been prepared by the Medical Technologies Evaluation Programme team to highlight the significant findings of the External Assessment Centre (EAC) report. It summarises additional clinical and economic evidence along with any other relevant changes since the guidance was developed. It should be read along with the Company submission, original assessment report and the assessment report update. The assessment report update overview forms part of the information received by the Medical Technologies Advisory Committee when it updates its recommendations on the technology.

Key issues for consideration by the Committee are described in section 7, following the brief summaries of the clinical and cost evidence.

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

- Appendix A: Sources of evidence
- Appendix B: Comments from professional experts
- Appendix C: Company claimed benefits
- Appendix D: Decision problem from the scope

1 Current guidance

Medical technologies guidance on GreenLight XPS for treating benign prostatic hyperplasia (MTG29) was issued in June 2016. The recommendations of the original guidance were as follows:

1.1 The case for adopting GreenLight XPS for treating benign prostatic hyperplasia is supported in non-high-risk patients. GreenLight XPS is at least as effective in these patients as transurethral resection of the prostate (TURP) but can be more often done as day-case procedure, following appropriate service redesign.

1.2 There is currently insufficient high-quality, comparative evidence to support the routine adoption of GreenLight XPS in high-risk patients, that is those who:

- *Have an increased risk of bleeding or*
- *Have prostates larger than 100ml or*
- *Have urinary retention.*

NICE recommends that specialists collaborate in collecting and publishing data on the comparative effectiveness of GreenLight XPS for high-risk patients to supplement the currently limited published evidence.

1.3 Cost modelling indicates that in non-high-risk patients, cost savings with GreenLight XPS compared with TURP are determined by the proportion of procedures done as day cases. Assuming a day-case procedure rate of 36% and that the GreenLight XPS console is provided at no cost to the hospital (based on a contracted commitment to fibre usage), the estimated cost saving is £60 per patient. NICE's resource impact report estimates that the annual cost saving for the NHS in

England is around £2.3million. In a plausible scenario of 70% of treatments being done as day cases, the cost saving may be up to £3.2million.

1.4 *NICE recommends that hospitals adopting GreenLight XPS plan for service redesign to ensure that day-case treatment can be delivered appropriately.*

With regard to high-risk patients, section 3.22 of the guidance states:

The committee noted that published evidence to support the use of GreenLight XPS in high-risk patients was limited in quantity and quality. The committee was advised by experts that in high-risk patients, TURP would often not be considered and that GreenLight XPS offers a safe alternative to TURP. The committee was advised that, because TURP is not normally used in high-risk patients, randomised studies compared with TURP in this group of patients are not considered ethical. The committee therefore concluded that multicentre prospective studies with GreenLight XPS were needed in this population.

2 Changes since publication of guidance

2.1 The technology

GreenLight XPS (Boston Scientific) is a 180 W, 532nm wavelength laser system for treating benign prostatic hyperplasia (BPH). It works by removing excess prostate tissue using laser vaporisation. The GreenLight XPS system consists of a laser console and a fibre optic delivery device.

The technology is available in the UK. The Company has confirmed that there have been no changes to the technology since MTG29 was issued. No new indications or applications not covered by the original guidance have been declared by the Company or identified by the EAC in view of the assessment

report update (ARU). There have been no changes to the pricing of GreenLight XPS console or consumables.

2.2 Current management

Current surgical treatment options for BPH when conservative management options have been unsuccessful or are not appropriate are found within the NICE Guideline on LUTS (CG97, 2015). This guideline was reviewed in November 2019 and is currently scheduled for update (CG97 review decision). Current treatment options include the following:

- Monopolar or bipolar transurethral resection of the prostate (TURP) (NICE has also published Medical technologies guidance on the bipolar system, PLASMA [MTG53])
- Transurethral vaporisation of the prostate (TUVP)
- Holmium laser enucleation of the prostate (HoLEP)
- Transurethral incision of the prostate (TUIP) (for prostates estimated as smaller than 30 ml)
- Open prostatectomy (OP) (for prostates estimated as larger than 80 ml).

More recently, alternative surgical approaches including prostatic urethral lift (PUL), water vapour thermal therapy, transurethral resection and haemostasis of the prostate and photoselective laser vaporisation techniques have been demonstrated to be alternatives each in their own indications. NICE has published Medical technologies guidance on some of these technologies including Rezum (MTG49) and Urolift (MTG58).

GreenLight XPS in the current care pathway: Current international Guidelines recommend GreenLight XPS as a treatment option for those who are at higher risk of bleeding (The European Association of Urology, 2021, The Canadian Urological Association, 2018, The American Urological Association, 2021).

GreenLight XPS is one of four technologies for the treatment of benign prostatic hyperplasia which is supported by NHS England MedTech Funding Mandate (2022/23)

The initial GreenLight XPS Guidance (MTG29; 2016) supported the use of GreenLight XPS as an alternative to bipolar or monopolar TURP or HoLEP for treating BPH in patients not considered of high-risk. The Company submitted new evidence for GreenLight XPS which was published since the initial guidance in 2016.

3 Company claimed benefits and decision problem

Details of the Company's claimed benefits are described in Appendix C. The decision problem is described in Appendix D.

4 Clinical Evidence

4.1 Summary of evidence of clinical benefit

Original Guidance (2016): The evidence base for the original guidance for GreenLight XPS (MTG29; 2016) was based on a single trial that compared GreenLight XPS with TURP (the GOLIATH study: Bachmann et al.2014, Bachmann et al. 2015, Thomas et al.2015). The EAC identified 7 studies of GreenLight XPS in the high-risk populations of interest (4 reported on people with larger prostates and 3 reported with people on anticoagulant therapy). Six of these studies were retrospective and there were no controlled studies, see sections 3.9 to 3.15 of the original assessment report for further details of each study in the high-risk populations. There were no studies located using GreenLight 180 W for patients with urinary retention.

In the original assessment report, the EAC reported that there was insufficient evidence to show any notable differences in effectiveness or adverse events in the high-risk population. As a result, the committee concluded that adopting

GreenLight is likely to be cost saving in non-high-risk patients however the published evidence was not sufficiently robust to support a recommendation for its routine use in high-risk patients.

Guidance review: Following review of the original guidance and published evidence since its date of issue, NICE decided to update the guidance (Review decision, 2019). This was to allow the medical technologies advisory committee to consider the new evidence on GreenLight XPS and its use in all patients including those considered high-risk patients (as proposed in the original guidance) which includes those who:

• have an increased risk of bleeding or

• have prostates larger than 100 ml or

• have urinary retention

Guidance update: The Company did a literature search and identified a total of 65 studies they considered were relevant for this guidance update. The EAC critiqued the Company's search strategy and carried out an independent search using an adapted version of search strategy used for the original guidance assessment report (MTG29) and informed by NICE MT564 Final Scope, 2021. Further details of the EAC's search strategy and its critique of the Company's search strategy can be found in Section 4.1 of the Assessment Report Update.

The EAC included 25 of the 65 studies identified by the Company and excluded 40, these are listed in Table 1, summary of included and excluded studies. Further details of reasons for exclusion can be found in Appendix A4 Assessment Report Update. As part of their literature search, the EAC also identified 10 systematic reviews. After reviewing the primary included in the reviews (n=54) 6 studies were deemed in scope (further details of these studies are found in Appendix A5, Assessment Report Update).

The EAC identified a total of 58 publications which were relevant to the decision problem and reported on outcomes defined in the scope (MT564 Final Scope). Further details of which can be found in Section 4.2 of the Assessment Report Update.

Table 1. summary of included and excluded studies

Studies included by EAC (n=58)	
Publication and study design	• 1 RCTs (Abolazm et al, 2020). • 3 propensity matched cohort (Azizi et al, 2017. Cimino et al, 2017. Castellani et al, 2018). • 2 prospective non-randomised (Hibon et al, 2017, Mattevi et al, 2020) • 5 retrospective non randomised (Cindolo et al, 2017. Reimann et al, 2019, Mathieu et al, 2017. Gondran-Tellier et al, 2021. Mesnar et al, 2021) • 8 prospective cohort studies (Gasmi et al, 2021, Ghahhari et al 2021, Tao et al, 2019, Berquet et al, 2015, Huet et al, 2019, Lopez et al, 2016, Akhtar & Raina 2018, Ferrari et al, 2021 • 38 retrospective cohort studies (Campobasso et al, 2020, Meskawi et al, 2017, Meskawi et al, 2019, Lee et al, 2016, Waters et al, 20121, Knapp et al, 2017, Goueli et al, 2021, Xu et al, 2021, Eken & Soyupak, 2018, Law et al, 2021, Rajih et al, 2017, Trujillo et al, 2021, Castelluci et al, 2020, Reimann et al, 2018, Zhou et al, 2017, Liu et al, 2020, Ghahhari et al, 2018, Aboutaleb et al, 2018, Chen & Chiang et al, 2016, Thomas et al, 2019, Trail et al, 2021, Reale et al, 2020, Barco-Castillo et al, 2020, Bausch et al, 2020, Campobasso et al, 2021, Pierce et al, 2021, Ajib et al, 2018, Bastard et al, 2017, Moiroud et al, 2019, Castellan et al, 2019, Plata et al, 2021 Hu et al, 2016, Destefanis et al, 2021, Contreras et al, 2021, Hermanns et al, 2019, Sun et al, 2018, Valdivieso et al, 2018, Marchioni et al 2018, • 1 case report (Barco-Castillo et al, 2019)
Studies in Company submission excluded by EAC (n=40)	
Publication and reason for exclusion	• 20 excluded as not being appropriate intervention (Bajic et al, 2019, Brant et al, 2020, Culkin et al, 2014, Elshal et al, 2020, Ferrari et al, 2021, Frendl et al, 2021, Gilfrich et al, 2021, Kiba et al, 2020, Kini et al 2020, Kobayashi et al, 2021, Laine-Caroff et al, 2021, Misrai et al 2016, Panthier et al, 2020, Proudhomme et al, 2020, Sachs et al, 2020, Stone et al, 2016, Sun et al, 2019, Vanalderwerelt et al, 2021, Yoo et al, 2017, Yu et al, 2021 • 17 excluded due to study design (Cacciamani et al, 2019, Castellani et al, 2021,Gomez-Sancha et al, 2015, Gravas et al, 2021, Gu et al, 2020, La Russa et al, 2021, Leonardo et al, 2020, Misrai et al, 2015, Nguyen et al, 2020, , Nguyen et al, 2021, Peng et al, 2020, Rapisarda et al, 2019, Salciccia et al, 2021, Schwarz et al, 2021, Soans et al, 2020, Zheng et al, 2019, Zhou et al, 2021, • 2 excluded due to language (Knoblauch et al, 2019, Thoulouzan et al, 2017 • 1 excluded due to comparator (Lanchon et al, 2018)
***Abbreviations**: RCT randomised controlled trial. EAC external assessment centre*	

Of the 58 studies, a total of 50 included high-risk patients (86%). Given the large volume of evidence, the EAC prioritised 37 of the 58 studies. The detail of these studies is listed in Tables 3a, 3b and 3c of the Assessment Report Update. The EAC considered the remaining 21 single arm studies in scope, however these single arm studies did not report on rare adverse outcomes or day-case procedures and were therefore not summarised or critically appraised in the Assessment Report Update

37 prioritised studies included:

- 11 comparative studies (1 RCT, 3 propensity matched cohort studies, 2 prospective non-randomised studies, 5 retrospective non-randomised studies). Four of these studies used GreenLight in both the study groups and compared them across different surgical techniques (including the only RCT, Abolazm et al.2020). Details of the comparative studies are reported in further detail in Table 2 below.

- 8 cohort studies including reporting in high-risk group population or as a subgroup

- 1 cohort study which reported the use of GreenLight as a day-case procedure

- 17 single arm studies reporting on rare adverse events outcomes only.

Table 2: Comparative studies selected by the EAC (n=11)

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Abolazm *et al.* (2020) †Egypt	RCT (n=49 randomised) Intervention: Ejaculatory hood-sparing GreenLight XPS 180 W PVP (n=25) ☒☑ Comparator: Standard GreenLight XPS 180 W PVP (n=24) ☑	Patients with LUTS secondary to benign prostatic obstruction in whom medical treatment failed (3 months) between Nov 15 and Sep,17. Setting: single centre, single surgeon	Primary: preserved AE at 1 year, change in sexual function, ejaculatory function, IIEF-15 score. Secondary: degree of LUTS relief (IPSS), Qmax, PVR, PdetQmax, bladder outlet obstruction index, complications, retreatment. ☑	Comparison of surgical technique (standard photoselective vaporisation vs. ejaculatory hood sparing vaporisation).
Azizi *et al.* (2017) Canada & USA	Propensity matched retrospective cohort, (n=444) Intervention: GreenLight XPS 180 W PVP (n=222) ☑ Comparator: GreenLight XPS 180 W vapour-resection/vaporincision technique (n=222) ☑	Patients with LUTS secondary to BPH, treated with laser prostatectomy between August 2021 and August 2014. Setting: Multi-centre (N=5); 5 surgeons	Changes in IPSS, QoL, PVR, Qmax, PSA measured at 6 months, complications and adverse events. ☑	High-risk (includes patients on anticoagulation, patients with preoperative urinary retention and patients with prostate volume >100 ml, but not exclusively).
Cimino *et al.* (2017) †Italy	Propensity matched cohort (n=110 included for analysis: use of propensity score matching based on prostate volume, peak flow, IPSS) Intervention: GreenLight XPS 180 W PVP (n=55) ☑ Comparator: TURP (n=55) ☑	Consecutive patients undergoing PVP or TURP for relief of LUTS between January 2014 and January 2016. Setting: multi-centre (N=2)	Primary: BPH6 endpoint which is a composite of 6 elements Secondary: IPSS, SHIM, Qmax.☑	Non-randomised comparison of TURP and GreenLight PVP (propensity matched).

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Castellani *et al.* (2018) Italy	Propensity matched (n=90) Intervention: GreenLight XPS 180 W (n=291) ☑ Comparator: ThuVEP (RevoLix Duo 90W) with morcellator (n=214) ☒☑	Consecutive patients undergoing surgery for BPH between 2014 and 2017, according to EAU guidelines. Setting: multi-centre (N=3 for GreenLight, different single centre for ThuVEP); multiple surgeons (NR)	IPSS, Qmax, duration of catheterisation, QoL, LoS, readmission, blood loss, complications. ☑	High-risk (includes patients taking antiplatelet and anticoagulation, history of indwelling catheter but not exclusively). Comparator (ThuVEP) out of scope.
Hibon *et al.* (2017) France	Prospective non-randomised (n=106) Intervention: GreenLight XPS 180 W PVP (n=55), Comparator: GreenLight XPS 180 W anatomical vaporization (n=51) ☒☑	Patients undergoing standard or anatomical PVP as treatment for large prostate enlargement (prostates >80cm^3) between 1st December 2012 and 1st December 2013. Setting: multi-centre (N=2); 2 surgeons	LoS, catheterisation time, complications, change in IPSS, PSA, Qmax, PVR, prostate volume, and urinary QoL at 1, 3, 6 & 12 months. ☑	Comparison of surgical technique (GreenLight PVP versus anatomical vaporisation). High-risk (patients taking anticoagulation, prostate volume >100 ml, with catheter in place, but not exclusively).
Mattevi *et al.* (2020) Italy	Prospective non-randomised (n=100) Intervention: GreenLight XPS 180 W PVP (n=50) ☑ Comparator: TURP (n=50) ☑	Consecutive patients undergoing surgical treatment of BPH between March 2015 and March 2016, captured in prospectively maintained database. Setting: single centre; 2 urologists per arm	IPSS, Qmax, PVR, duration of catheterisation, LoS, complications, retreatment and re-catheterisation rates, transfusion rates, dysuria.☑	High-risk (includes patients taking anticoagulation/antiplatelets but not exclusively)
Cindolo *et al.* (2017) Italy	Retrospective non-randomised (n=813) Intervention: GreenLight XPS 180 W, either standard PVP (n=403) or Comparator: anatomical PVP (n=410); via surgeon preference. ☑	Patients undergoing standard and anatomical PVP between 2011 and 2016. Setting: multi-centre (N=14); multiple surgeons (NR)	IPSS, Qmax, duration of catheterisation, QoL, LoS, readmission, blood loss, capsular perforation, complications. ☑	High-risk (includes patients with indwelling catheter, prostate volume >100 ml, and patients taking antiplatelet or anticoagulation therapy, but not exclusively).

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Reimann *et al.* (2019) Germany	Retrospective non-randomised (n=254) Intervention: GreenLight XPS 180 W PVP (n=140) ☑ Comparator: TURP (n=114) ☑	Patients who underwent PVP or TURP for symptomatic BPE between June 2010 and February 2015. Setting: single centre; multiple surgeons (NR)	LoS, prolonged hospital stay (>2 days PVP, >4 days TURP), catheterisation duration, complications (<30, 30-180, and >180 days) reintervention, patient satisfaction, IPSS-QoL ☑	High-risk (patients taking anticoagulation and with urine retention, but not exclusively)
Mathieu *et al.* (2017) France	Retrospective non-randomised (n=237) Intervention: GreenLight XPS 180 W (n=51), monopolar TURP (n=99), HoLEP or ThuLEP (n=64), open prostatectomy (n=23) ☒☑	Data from 20-30 consecutive patients undergoing surgical treatment for LUTS related to BPH (following EAU guidelines) between January 2012 and June 2013 were included. Setting: multi-centre (N=9) included 2 private centres, multiple surgeons (NR)	LoS, readmission, complications, costs ☑	High-risk (includes patients with prostate volume >100 ml, urinary retention with catheter preoperatively, and those taking antiplatelet or anticoagulation, but not exclusively). Some comparators (ThuLEP combined with HoLEP, open prostatectomy) out scope.
Gondran-Tellier *et al.* (2021) France	Retrospective non-randomised (n=171) Intervention: 180 W PVP, assumed GreenLight XPS (n=62), - monopolar or bipolar TURP (n=48), - endoscopic enucleation via Comparator: GreenLEP 80 W or HoLEP (n=21), - prostate artery embolisation (n=15), - open prostatectomy (n=25) ☒☑	Patients with refractory urinary retention despite the use of α-blocker and trial without catheter who underwent surgery for BPO between January 2017 and January 2019. All patients had preoperative urinary catheter. Setting: multi-centre (N=3), multiple surgeons (NR)	LoS, success of catheter removal, catheter-free survival, retention recurrence, reoperation, complications ☑	High-risk (all patients have retention, also includes patients with prostate volume >100 ml and patients taking anti-thrombotics but not exclusively) Some comparators (GreenLEP combined with HoLEP, prostate artery embolization, open prostatectomy) out scope.

Author (year); location	Design and intervention(s)	Participants & Setting	Outcomes	EAC comments
Mesnard *et al.* (2021) France	Retrospective non-randomised (n=15) Intervention: GreenLight PVP XPS 180 W Comparator:TURP, prostatectomy ☒☑	Patients with haemophilia A or haemophilia B listed in database, who underwent prostate interventions (prostate biopsy, radical prostatectomy, radiotherapy, simple prostatectomy, TURP, GreenLight PVP) between 1st January 1997 and 1st September 2020. Setting: single centre; surgeons (NR)	Blood loss, complications, LoS, duration of catheterisation, readmission ☑	High-risk (exclusively in haemophilia patient group).

Key: ☑ aspect of study in scope; ☒ aspect of study not in scope; ☑☒ aspect of study partially in scope, or elements of this are not in scope; † assumed from author affiliations (not explicitly stated in paper).

Abbreviations: AAT, antithrombotic therapy; aPVP, anatomical photoselective vaporisation of prostate; ASA, American Society Anesthesiology; BCI, bladder contractility index; BMI, body mass index; BOO, bladder outlet obstruction; BPH, benign prostatic hyperplasia; BPO, benign prostatic obstruction; DUA, detrusor underactivity; EAC, external assessment centre; Hb, haemoglobin; Ht, haematocrit; IIEF-5, International Index of Erectile Function; IIEF-15, International Index of Erectile Function-15; IPSS, international prostate symptom score; ISI, incontinence severity index; LoS, length of stay; LUTS, lower urinary tract symptoms; MSHQ-EjD, Male Sexual Health Questionnaire; NR, not reported; RCT, randomised controlled trial; PEBE, photoselective en-bloc enucleation; PGI-I, patient global impression of improvement; PSA, prostate specific antigen; PVP, photoselective vaporisation of prostate; PVR, post-void residual volume; QoL, quality of life; SHIM, sexual health inventory for men; TRUS, transrectal ultrasound; TURP, transurethral resection of the prostate; UDS, urodynamic study; UTI, urinary tract infection; VAS, visual analogue scale.

4.2 EAC critique of new evidence

The EAC identified a large volume of evidence (n=58) specifically using GreenLight XPS 180 W console since the original assessment report. The clinical evidence included was considered to be low to good quality. As discussed, the EAC focused on the 37 studies most relevant to the decision problem (comprising of 1 RCT, 3 propensity matched cohorts, 7 non-randomised, non-propensity-matched comparative studies, and 26 cohort studies stratifying patients by risk groups [N=8], procedure setting [N=1] or those which reported on rare adverse events [N=17]).

The GOLIATH trial, which was considered within the original Assessment Report, remains the only randomised evidence comparing GreenLight against TURP (mono- and bi-polar combined). No randomised evidence comparing GreenLight 180 W PVP to HoLEP has been identified.

Eleven comparative studies were identified, however 4 of these included GreenLight in both the study groups in order to compare different surgical techniques (this included the only RCT, Abolazm et al, 2020; these studies were considered not directly relevant to the decision problem). The remaining 7 non-randomised comparative studies compared GreenLight photoselective vaporization of the prostate (PVP) with other surgical procedures (TURP, Holmium laser enucleation of the prostate HoLEP, Thulium laser enucleation of the prostate ThuLEP, prostate artery embolisation PAE, open prostatectomy). The 7 comparative studies included 2 propensity matched cohort studies (Azizi et al, 2017, Cimino et al, 2017), 1 prospective non-randomised study (Mattevi et al, 2020), and 4 retrospective non-randomised studies (Reimann et al, 2019, Mathieu et al, 2017, Gondran-Tellier et al, 2021, Mesnard et al, 2021). Duration of follow-up in 4 of the 7 studies was limited to 12 months and not explicitly reported in the other 3 studies.

Results

Based on the comparative evidence, the EAC stated that GreenLight is associated with shorter duration of catheterisation (Reimann *et al.* 2019;

Cimino *et al.* 2017; Mattevi *et al.* 2017), and duration of hospital stay (Gondran-Tellier *et al.* 2021; Reimann *et al.* 2019; Mathieu *et al.* 2017; Mattevi *et al.* 2017) when compared with TURP, however these are not UK based and therefore may not be generalisable to the NHS. Quality of life measures were generally poorly reported; one propensity matched cohort study (Cimino *et al.* 2017) reported significantly higher ejaculatory function at 12 months with GreenLight than TURP.

Results from the clinical evidence suggest that GreenLight 180 W XPS PVP can provide symptomatic relief of LUTS in patients with BPH including in patients considered of high-risk (prostate volume greater than 100 ml, patients with preoperative urine retention, patients at risk of bleeding), with low occurrence of device-related adverse events. Twelve studies reported on the proportion of patients requiring blood transfusion; between 0% and 2.2% intraoperatively, and between 0.6% and 0.8% within 30 days. Seventeen studies recorded the proportion of patients experiencing capsular perforation; no events occurred in six studies, and range between 0.1 and 5.6% in the remaining studies. Transurethral resection syndrome was only identified in one patient across all included studies.

Long-term evidence from single-arm studies (n=17) demonstrates that improvements in International Prostate Symptoms Score (IPSS), Quality of Life (QoL), Photoselective Vaporisation of the prostate (PVR) and maximum flow rate (Qmax) are sustained up to 60 months post-operatively when compared to baseline. However, due to the lack of randomised evidence, the EAC was unable to conclude long-term efficacy of GreenLight when compared with other surgical interventions such as HoLEP or TURP.

Results in high-risk populations

The majority of evidence published since NICE guidance on GreenLight (MTG29, 2016) has included high-risk patients within their recruitment (50 of 58 studies). However only 4 studies reported high-risk populations exclusively, including 2 retrospective non-randomised comparative studies (Gondran-

Tellier *et al.* 2021; Mesnard *et al.* 2021) and 2 retrospective cohort studies (Meskawi *et al.* 2017; Eken & Soyupak *et al.* 2018).

People who have an increased risk of bleeding: Four cohort studies stratified by anticoagulation status (Lee et al 2016, Knapp et al 2017, Meskawi et al 2019, Eken & Soyupak et al, 2018). One study (Lee et al, 2016) reported a higher rate of conversion to TURP in patients on anticoagulation (13.5% versus 6.1%, p=0.01), however as anticoagulation is associated with comorbidities it is not possible to directly attribute causation to GreenLight XPS intervention. Three studies reported on length of hospital stay (Meskawi et al. 2019; Lee et al. 2016; Knapp et al. 2017). Across all 3 studies, people on anticoagulation therapy had statistically significant longer length of hospital stay compared with those not on anticoagulation (p values p<0.02). Readmission was reported as significantly higher in antiplatelet and anticoagulation medication group (p=0.02) in Meskawi et al 2019. Two studies reported the duration of catheterisation to be significantly higher in antiplatelet and anticoagulation groups (Knapp et al 2017 and Meskawi et al 2019**).**

People who have a large prostate size: One retrospective cohort study (Campobasso *et al* 2020) subgrouped patients by prostate size (n=1031 patients, 916 with prostate volume less than 100 cc, 115 greater or equal to 100 cc); however, 16.3% had a history of indwelling catheter (with a significant difference in the proportion across subgroups). This study reported no significant difference in IPSS, Qmax, length of post-operative stay, duration of catheterisation and post-operative acute urine retention between subgroups. Patients with prostate volume >100 ml had a higher incidence of early (50.4% vs 34.7%) and late complications (21.7% vs 12.8%).

People who have urinary retention: Only one retrospective cohort study (Goueli et al, 2017) subgrouped patients by preoperative urine retention status (n=322, 137 with preoperative urine retention and 195 without). There were significant differences in baseline measures in the subgroups, with the preoperative retention group including significantly larger prostates (76ml vs 69ml; p<0.001) and significantly higher ages (70 years vs 66 years; p=0.001).

The study reported no significant difference in IPSS, Qmax, PVR and QoL between the urinary retention subgroups. The rate of complications was higher (but not significantly) in the non-retention group, specifically at 90 days (35.4% vs 21.2%; p=0.009).

Experts reported that urinary retention may not be considered as a high-risk factor in clinical practice (EAC Correspondence Log, 2022), with one Clinical expert suggesting that nearly 50% of patients having surgery for BPH have urinary retention. This is further supported by the BAUS Bladder Outflow Obstruction Audit (2019), which reports the indication for surgery in 43% was acute or chronic urinary retention (EAC Correspondence Log, 2022).

Adverse Events: Safety outcomes identified from the clinical evidence has been summarised in Section 5 of the Assessment Report Update. There were no adverse events related to patient harm and no safety signals of concern on GreenLight XPS practice across the population.

There is a large amount of evidence on safety and efficacy, and in clinical guidelines (EUA, CUA, AUA) supporting the continued use of GreenLight XPS 180 W PVP for treating patients with BPH. Whilst occurrence of adverse events is low even in high-risk groups, availability of blood (in patients requiring a transfusion) and beds (in patients requiring increased observation) are advised.

4.3 Integration into the NHS

There is consensus among Clinical experts and the literature that GreenLight XPS 180 W PVP can be undertaken as a day-case procedure within an NHS setting (EAC Correspondence Log; Trail *et al.* 2019). The proportion of GreenLight XPS procedures that are conducted as day-case procedures varied in clinical practice; one expert estimated 25% of procedures were conducted as day-case, one expert estimated 40% to 60%, five experts estimated between 80% to 90% (EAC Correspondence Log, 2022). The proportion of patients undergoing GreenLight XPS intervention as a day-case procedure was reported in 4 studies, ranging between 36.5% and 90%.

Clinical experts suggested that in some circumstances day-case procedures may not be suitable, including individuals with high anaesthetic risks, frailty, social reasons and comorbidity status (EAC Correspondence Log, 2022)

Eight of 11 Clinical experts suggest GreenLight XPS procedure would be particularly beneficial in patients considered at high-risk, elderly or on anticoagulation therapy (EAC Correspondence Log, 2022). When considering integration in practice, 4 experts stated that lack of training could be a potential barrier to adoption across the wider NHS (EAC Correspondence Log, 2022). The Company reports that training continues to be provided by centres of excellence in conjunction with Boston Scientific.

The adoption of GreenLight XPS may also require Trusts to invest in additional safety equipment on the advice of their Laser Safety Officer in keeping with the IFU which states everyone in the room is required to wear protective eye wear specific to the wavelength of its green length (532nm).

4.4 EAC Conclusions from new clinical evidence

Clinical experts agreed that GreenLight 180 W XPS PVP is used routinely in the NHS including in high-risk populations and in day-case procedures (EAC Correspondence Log, 2022). No additional randomised evidence has been published since the original assessment report.

GreenLight PVP is associated with a significantly shorter post-operative catheterisation period (Reimann *et al.* 2019; Cimino *et al.* 2017; Mattevi *et al.* 2017), significantly shorter hospital stay (Gondran-Tellier *et al.* 2021; Reimann *et al.* 2019; Mathieu *et al.* 2017; Mattevi *et al.* 2017), and significantly higher ejaculatory function at 12 months (Cimino *et al.* 2017) when compared with TURP. However as none of these studies were conducted in a UK setting, results may not be generalisable to the NHS.

The new evidence continues to support the use of GreenLight 180 W XPS as an available option in patients with BPH for symptomatic relief, with its clinical benefits also realised in high-risk patient groups (prostate volume greater than

100 ml, patients with preoperative urine retentions, patients at risk of bleeding) with low occurrence of adverse events.

5 Summary of economic evidence

5.1 Published studies

The EAC's independent literature search identified 6 economic studies (documented in Table 16, Assessment report update). None of the studies were reported in the UK or NHS setting. All studies included GreenLight XPS with TURP or HoLEP as comparators. None of these studies reported on high-risk groups exclusively, two reported on high-risk criteria in the study (Mathieu et al, 2017 included patients with prostates greater than 80ml, those with urinary retention and on anticoagulation therapy, Masucci et al.2018 reported on anticoagulation therapy status).

Two of the six studies found GreenLight XPS to be cost-saving compared with TURP (Masucci et al. 2018, Ulchaker and Martinson 2018). Cost savings were driven by reduction in readmissions and length of stay including performing day-case procedures. One study found GreenLight to be more cost-effective than TURP (Caicedo et al. 2019), whereas two studies reported TURP to be more cost-effective (Erman et al. 2018, Ulchaker and Martinson 2018). One study reported GreenLight to be more costly than TURP and HoLEP or ThuLEP in patients with prostate volume less than 80 ml, but cost-saving compared to HoLEP or ThuLEP in patients with prostate volume greater than 80 ml (Mathieu et al. 2017). Further details of these studies can be found in Section 9.1 of the Assessment Report Update.

5.2 Cost modelling

This guidance update includes considerations of 2 economic models:

- Model 1 is an updated version of the de novo decision tree model used in the original guidance

- Model 2 is a new de novo Markov model submitted by the Company (December 2021) during guidance update.

5.2.1 Model 1 – Updated original economic model

Model structure: The EAC reviewed the original model updated by Birmingham and Brunel EAC during development of the original guidance (EAC Assessment Report, 2015). This is a decision tree model, in which a patient undergoes an intervention (Greenlight XPS compared with TURP and HoLEP) as either a day-case or inpatient. Following this, the endpoints are the occurrence of no complications, grade two complications, or grade three complications, within six months after the intervention. The EAC felt this time horizon of six months remained appropriate for safety outcome measures, as most complications would still be expected to occur in this period, however a longer time horizon would be beneficial for efficacy outcomes.

The assumptions in the original Economic Submission were discussed in the Assessment Report by Birmingham and Brunel EAC (AR, 2016). The EAC used data from the GOLIATH trial to inform the percentage of people having GreenLight XPS as a day-case procedure. Clinical outcomes are informed by the GOLIATH trial and included patients with prostates over 100 ml and patients with increased risk of bleeding, however outcomes were not reported exclusively. During exploration of the original model as part of the Guidance update process the EAC (NuTH) noted errors in some of the clinical parameters applied in the EAC base case, however they reported the impact on total cost differences were minimal (details of these are presented in section 9.2 Assessment Report Update).

Model parameters: Clinical outcomes (including safety, efficacy and operation times) included in the model were informed by the GOLIATH trial and unchanged from the original assessment report. The Company confirmed the cost of GreenLight XPS was unchanged from the original assessment report (EAC Correspondence Log, 2022). Day-case procedure rates of

35.96% for both GreenLight and HoLEP, and 4.08% day-case procedures with TURP were used from the original model.

Key changes made by the EAC:

- **Excess bed days:** The EAC noted that none of the newly available evidence (including NHS activity reports from 2019-2020) identified patients staying in hospital beyond 5 days (previously reported excess bed days), so the EAC removed excess bed days from the original economic model (cost of £294.00 in original model).
- **Mean length of stay (LoS):** The mean LoS applied in the original economic model were 10.36 days for HoLEP and GreenLight and 10.65 for TURP. The EAC amended mean length of stays to 2.3 days for TURP and 1.6 days for GreenLight and HoLEP based on NHS activity data from 2019/20. However, acknowledged the limitation that GreenLight and HoLEP could not be differentiated from each other using current clinical coding.

- **Capital costs of HoLEP**: calculated cost for HoLEP significantly reduced from the original guidance (from £1,040.96 to £49.44). This was calculated considering the cost of single use and reusable fibres, cost of the device and the number of patients treated per year (which had increased from 25 to 250 in 2021) in line with the approach taken in other BPH technology assessments by NICE.

- **Technology costs**: The EAC used technology costs from the recent assessment report for MTG 49 (EAC Assessment Report, 2019) to reflect inflation across the comparators**.**

All updated parameters and costs are described in Section 9.2 and Table 17 of Assessment Report Update.

Results: The updated base case results from the original assessment report (EAC Assessment Report, 2015), are shown in Table 4 below. Further detail of the cost breakdown informing this is reported in Section 9.3 Assessment

Report Update (Table 18b, Table 19b, Table 20).

Table 4: Summary of Model 1 - Original guidance base case updated cost savings for GreenLight versus TURP and HoLEP

	Cost saving per patient	
	TURP	HoLEP
Base Case, 2016 Corrected	-£60.19	-£851.13
Base Case Updated 2022	-£69.94	+£114.43

Applying updated costs, the EAC has found that GreenLight XPS remains cost-saving when compared with TURP. Cost-saving is uncertain against HoLEP. This is due to decreased capital costs (attributed per patient) associated with the increased use (per year) of HoLEP in the updated model.

Sensitivity analysis: The EAC considered that there remains significant uncertainty regarding the proportion of patients undergoing prostate interventions for BPH as a day-case procedure because of lack of comparative data in the UK. Only one single-arm UK study reported 68% of GreenLight procedures as day-case procedures (Trail *et al.* 2021). Four Clinical experts agreed with 68% of GreenLight cases being performed as day-case procedures and three Clinical experts were unsure of the proportions (EAC Correspondence Log, 2022). Two additional Clinical experts suggested alternative figures, with one expert noting 90% of GreenLight being performed as day-case and another noting 20% as a more realistic figure (EAC Correspondence Log, 2022). Four Clinical experts agreed with the TURP and HoLEP day-case parameters used in the original model (36% and 4% HoLEP and TURP, respectively), but three additional experts suggested the proportion undergoing day-case TURP should be higher than 4% (ranging from 4 to 20%). One also suggested a higher day-case proportion in patients undergoing HoLEP (suggesting a range of 35 to 60%). Due to the lack of consensus among experts the EAC carried out univariate sensitivity analysis

(Table 21, Assessment Report Update). Results suggested when 68% of GreenLight were done as a day-case procedure, GreenLight had a saving of £373.01 and £188.63 compared with TURP (assuming 4.08% day-case rate) and HoLEP (assuming day-case rate remains at base case of 35.96%), respectively.

The EAC threshold analysis (detailed in Section 9.3, figure 1, Assessment report update) reported that cost savings remain likely when compared with TURP but results were uncertain when compared to HoLEP:

- when GreenLight day-case procedures are maintained at 68%, the proportion of day-case procedures for TURP would have to exceed 43.6% before GreenLight would be considered cost-incurring; the EAC considered this unlikely clinically.

- The proportion of HoLEP day-case procedures would have to exceed 56% for GreenLight to be considered cost-incurring; the EAC considers this scenario is plausible, although within the upper range suggested by Clinical experts. One Clinical expert suggested HoLEP day-case procedures could range between 35% to 60%. Four experts agreed with the base case of 35.96% to be an accurate reflection of HoLEP day-case procedure rates (EAC Correspondence Log, 2022).

5.2.2 Model 2- New economic model

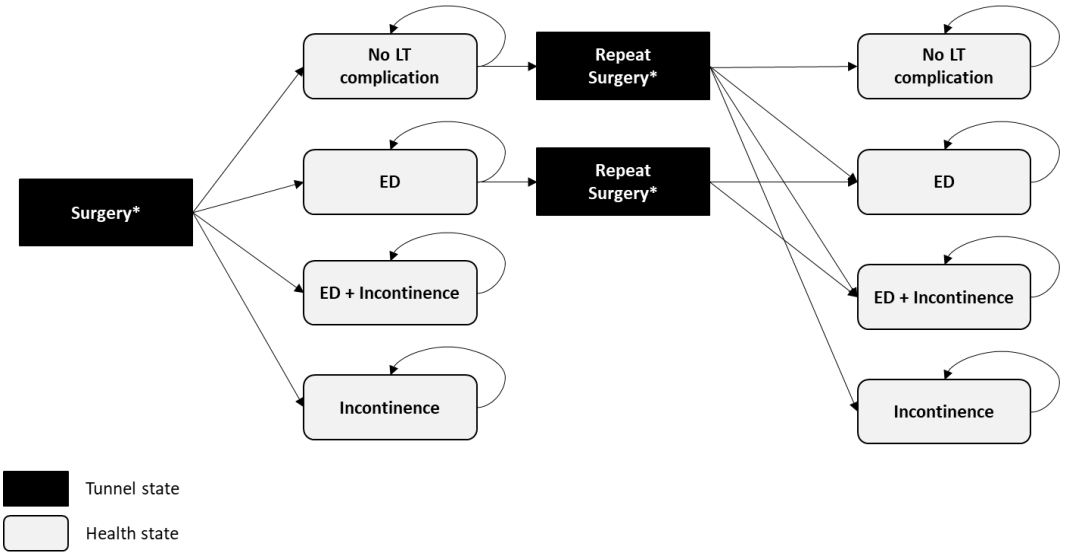
Model structure: An additional cost model was submitted by the Company during the guidance update. The model was a Markov model (see figure 1 below). The Company proposed that this model was more appropriate because it would:

- capture hospital costs more accurately for high-risk patients
- apply a more detailed approach to calculating and capturing a range of adverse events
- allow the use of 2019/20 costs compared to costs from the original model from 2015

- provide flexibility to select more than one comparator and use GreenLight as the intervention.

Whist some of these aspects could have been incorporated in the original decision tree model, the EAC considered that the main benefit of using the Markov model is the ability to model surgical retreatment (including potentially with a different intervention) and long-term needs.

Figure 1. Structure of updated economic model



Abbreviations: LT, long-term; ED, erectile dysfunction
*Surgical tunnel states include risk of short-term complications with surgery

The model is from a UK perspective, with a discount rate of 3.5% applied. The model employs a 4-year time horizon (which the Company reported was due to the availability of clinical data in 2020). The model was developed to include all people who need treatment for BHP and included a scenario for high-risk patients only. The assumptions of the model are summarised in Assessment Report Update Table 21.

The EAC identified errors in the Markov model and attempted to correct with the Company (detailed in Assessment Report section and Correspondence Log, 2022). Subsequently the Company submitted a second updated version addressing some errors, but there remained errors in the model (details are reported in Appendix E3 of the Assessment Report Update). The EAC

critiqued version 2 of the Markov model, using the Drummond checklist (Drummond et al. 1996, Assessment Report Update Appendix E2).

Model parameters: Data used to populate the high-risk scenario was derived from an unpublished systematic review that was provided by the Company. The Company confirmed the systematic review has been resubmitted for publication and remained unpublished by 20/04/2022 (EAC Correspondence Log, 2022). The definition of high-risk included in this study differed from the final scope NICE MT564 Final Scope, 2021). Some clinical parameters (surgical retreatment, non-acute urine retention, acute urine retention, bladder neck contracture or stricture, bleeding or need for blood transfusion, length of hospital stay) were changed to model the high-risk population, listed in Table 23 Assessment Report Update. These parameters were informed by the results from the unpublished systematic review.

The EAC critically appraised the unpublished systematic review which is reported in more detail in the Assessment Report Update (Appendix B4, Assessment Report Update). The EAC considered the unpublished systematic review to be low quality evidence due to a lack of transparency resulting in challenges verifying outcomes and a large heterogeneity across included studies preventing meta-analysis. The EAC thought that this data was not robust enough to estimate the cost impact of using GreenLight compared with TURP and HoLEP in high-risk patients.

The EAC replicated the Company base case model (all people with BPH), using R Programming language and rdecision package.

Changes made by the EAC

- **Time horizon:** The EAC considers a 5-year time horizon as more appropriate (than Company presented 4-year time horizon) to reflect the most robust comparative literature in the GOLIATH trial.

- **High-risk population:** given the lack of comparative, randomised evidence in high-risk groups the EAC considered that modelling all-

patients as more appropriate and more generalisable to UK NHS patients.

- **Clinical parameters:** the EAC used data from the GOLIATH trial instead of data from the unpublished systematic review data to inform the clinical parameters because it judged the GOLIATH study to be better quality and the most robust comparative evidence to date.

- **Interventions:** The proportion of patients undergoing mono-polar TURP applied was 38% using latest data from the BAUS Bladder Outflow Obstruction audit, 2019. The EAC also included 0.25% of GreenLight patients requiring conversion to TURP due to surgical complications based on clinical evidence, expert opinion and MAUDE data.

- **Length of stay:** updated from 10.36 days for HoLEP and GreenLight and 10.65 days for TURP down to 1.6 days for GreenLight and HoLEP and 2.3 days for TURP based on NHS activity data for 2019/20. Again, acknowledging that GreenLight and HoLEP cannot be differentiated using currently available clinical coding.

- **Technology costs:** The EAC updated technology costs across GreenLight, TURP and HoLEP to reflect inflation across all technologies for consistency (see Table 23 Assessment Report Update). The EAC did not include consumable costs for protective eyewear because they were deemed negligible (see Section 9.2 Assessment Report Update)

Results: Company and EAC cost savings in the Markov model are reported in Table 5 below.

Table 5. Model 2- Markov Model Company and EAC GreenLight cost savings against TURP and HoLEP

	TURP	**HoLEP**
Company reported cost savings for high-risk only population	-£1,556	-£753
EAC replication over 4 years (without cost of saline bladder irrigation)	-£631	-£712
EAC base case over a 5-year time horizon	-£304.83	-£269.52

Sensitivity analysis: The Company submitted sensitivity analysis including tornado diagrams to present univariate deterministic sensitivity analysis (DSA) and incremental cost difference curves for probabilistic sensitivity analysis (PSA) results. Sensitivity analysis reported:

- TURP cost-savings -£306 to -£2,785
- HoLEP cost-savings -£413 to -£1,185

The EAC was unable to replicate the PSA and verify the results independently of the updated Company model. The EAC found that the addition of the high-risk scenario had reduced the transparency of the economic model because of errors in the model. The EAC did trial several changes in the Company model (reported in Table 26 of the Assessment Report Update) and reported that the majority of scenarios (13 of 14) modelled on the general population demonstrated GreenLight to be cost-saving when compared to TURP and HoLEP at 4 years (See Table 25 Assessment Report Update).

The EAC conducted a PSA around its base case using a restricted number of parameters considered to be uncertain, including the proportion undergoing mono/bipolar TURP and procedure durations which demonstrated:

- GreenLight to be cost-saving against TURP -£894.41 to +£487.18 with 83.1% of simulations being cost-saving.

- GreenLight to be cost-saving against HoLEP -£1171.35 to +601.35 with 75.1% of simulations being cost-saving.

However, the EAC considered that the results of PSA were not robust because a lack of comparative or national audit data for key parameters. As a result, the EAC carried out additional univariate threshold analysis (presented in Figure 3. Assessment Report Update). This reported that:

- if the procedure duration of TURP and HoLEP reduced below 43.7 and 60.0 minutes respectively (relative to 49.6 minutes for GreenLight) GreenLight would become cost-incurring.

- if the length of hospital stay following TURP or HoLEP reduced below 1.5 and 0.9 days respectively (relative to 1.6 days for GreenLight) then GreenLight would become cost-incurring.

EAC conclusions on the economic evidence: Previous guidance (MTG29) highlighted the insufficient economic evidence to inform models assumptions in clinical and cost parameters, especially in the high-risk population, compared with HoLEP. The EAC identified 58 eligible studies published since MTG29 (2016), the majority of which included high-risk patients, with no major safety signal raised. The only randomised evidence comparing GreenLight to TURP remains the GOLIATH trial, with no additional follow-up reported than that described in the original MTG29. No randomised evidence has been identified which compares GreenLight to HoLEP.

The EAC considered that there remains significant uncertainty in current evidence regarding the proportion of patients undergoing prostate interventions for BPH as a day-case procedure, or length of stay due to lack of comparative data in the UK.

The EAC concluded both economic models (original decision tree and updated Markov model) including high-risk populations, demonstrate the potential for GreenLight to be cost saving when compared with TURP and

HoLEP. However, due to the lack of comparative evidence there remains some uncertainty regarding the magnitude of cost savings.

6 Ongoing studies

Eleven ongoing studies were identified and 4 completed with no associated publications (as of 09/12/2021). These are summarised in section 8.2 of the guidance assessment report update.

7 Implications for research

The majority of evidence published since NICE Guidance on GreenLight XPS (MTG29, 2016) has included high-risk patients. As reported in MTG29, the EAC highlights that, due to the increased risk of bleeding complications and longer hospital stays with TURP, further randomised studies comparing with GreenLight XPS in a UK NHS setting exclusively in high-risk patients are likely to be considered unethical.

Currently available clinical coding does not distinguish between types of BPH surgery or diagnosis codes such as high-risk groupings. Future service evaluation or multi-centre audit studies would help address the lack of data regarding procedure duration and length of stay.

8 Issues for consideration by the Committee

Clinical evidence

- The clinical evidence base has greatly increased since guidance publication with the majority including the high-risk patients, however comparative data and data reporting on high-risk populations exclusively are limited. Are the committee satisfied that the evidence supports the clinical benefits of GreenLight in these high-risk populations?

Cost evidence

- The EAC did not identify any appropriate data to inform the cost model for people with high-risk and presented a base case for the cost impact in all people treated for BHP informed by the GOLIATH study data (that included patients with prostate over 100 ml and patients with increased risk of bleeding).
    - Are the committee satisfied the EAC base case modelling is generalisable to the high-risk population of interest?
    - Is there a model that the committee feel is more appropriate to inform their decision making?
- The EAC highlighted uncertainties in both economic models in the following parameters across GreenLight, TURP and HoLEP procedures:
    - proportion of procedures done as day-case (decision tree) or length of stay (Markov model)
    - procedural duration

  Are the committee satisfied that the univariate threshold analysis effectively addresses these uncertainties?
- Are the committee satisfied the day-case procedure rates, procedure duration and length of stay for TURP and HoLEP which would result in GreenLight being cost-incurring are clinically unlikely?

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NICE Medical Technologies Evaluation Programme

February 2022

Appendix A: Sources of evidence considered in the preparation of the overview

Guidance update report:

Keltie K, Parker R, O'Leary R, Sims A, Bellios E, Garcia, S, Wallace S GreenLight XPS for treating benign prostatic hyperplasia, Guidance Update, January 2022

Current guidance:

GreenLight XPS for treating benign prostatic hyperplasia. NICE medical technologies guidance [MTG29] (2016) Available from www.nice.org.uk/guidance/MTG29

Guidance update scope

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Appendix B: Comments from professional bodies

Expert advice was sought from experts who have been nominated or ratified by their Specialist Society, Royal College or Professional Body. The advice received is their individual opinion and does not represent the view of the society.

Maya Harris
Consultant Urological Surgeon, South Warwickshire NHS Foundation Trust, BAUS, AUA, EAU, Royal College of Surgeons of England

Gordon Muir
Consultant Urologist, Kings College Hospital and London Bridge Hospitals

Richard Hindley
Consultant Urologist, Clinical Lead for Urology and Visiting Professor Hampshire Hospitals NHS Foundation Trust

Andrew Thomas
Consultant Urological Surgeon, Cwm Taf Morgannwg University Health Board Cardiff and Vale NHS Trust

Ian Pearce
Consultant Urological Surgeon, Manchester Royal Infirmary and Manchester University NHS Foundation Trust

Sanjay Rajpal
Consultant Urologist, Airedale NHS Foundation Trust

Aniruddha Chakravarti
Consultant Urological Surgeon, The Royal Wolverhampton NHS Foundation Trust

Marios Hadjipavlou
Consultant Urological Surgeon, Guys and St Thomas' NHS Foundation Trust

Amr Emara

Consultant Urologist, Hampshire Hospitals NHS Foundation Trust

Feras Al Jaafari

Consultant Urologist, NHS Fife

Iqbal Shergill

Consultant Urological Surgeon, Wrexham Maelor Hospital.

Dominic Hodgson

Consultant Urologist, Portsmouth Hospitals NHS Trust

David Rawlings

Clinical Scientist, Laser Protection Adviser, Newcastle upon Tyne Hospitals NHS Foundation Trust

For full details, please see the expert adviser questionnaire (EAQ) responses and EAC Correspondence log which are both included in the committee pack.

Appendix C: Company claimed benefits

The benefits of GreenLight XPS to patients by the Company are:

- Shorter hospital length of stay, because the GreenLight XPS procedure can be done as a day-case procedure
- Shorter duration of catheterisation
- Quicker return to normal activity following treatment
- Lower likelihood of rehospitalisation within 30 days post procedure
- Reduction in patient stress and anxiety because typically no overnight stay is needed
- Reduction in pain leading to improved quality of life
- May be used in patients with comorbidities; those older in age, taking anticoagulants, with larger prostates and with urinary retention.
- Reduced risk of excessive or severe bleeding, TUR syndrome
- Reduced requirement for blood transfusion

The benefits to the healthcare system claimed by the Company are:

- Procedure performed as a day-case rather than as an inpatient
- Reduced length of stay in hospital
- Reduced risk of adverse events from bleeding and transurethral resection of the prostate (TURP) syndrome
- Reduction in hospital readmissions within 30 days post procedure
- Reduced requirement for blood transfusion.

Appendix D: Decision problem from scope

Population	People with urinary outflow obstruction secondary to benign prostatic hyperplasia in whom surgical intervention is indicated, especially those with prostates that are larger than ≥30ml.
Intervention	Greenlight XPS Photoselective Vaporisation of the Prostate (PVP)
Comparator(s)	• Monopolar and bipolar transurethral resection of the prostate (TURP) • Holmium laser enucleation of the prostate (HoLEP)
Outcomes	The outcome measures to consider to be included: **Patient outcomes** • symptoms of BPH (International Prostate Symptom Score [IPSS] • change in prostate volume • maximum flow rate (Qmax) • post void residual volume (PVR) • duration of catheterisation • rate of dysuria (pain) • quality of life measures, e.g., International Prostate Symptom Score Quality of Life (IPSS-QOL) • preservation of sexual function **System outcomes** • length of hospital stay • frequency of completion as a day case • rate of re-admission • procedural blood loss and blood transfusion requirement **Adverse effects** • rate of transurethral resection syndrome (TUR) • rate of capsular perforation • device related adverse events
Cost analysis	Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be long enough to reflect differences in costs and consequences between the technologies being compared. Comparators: monopolar TURP, bipolar TURP and holmium laser enucleation of the prostate (HoLEP). Monopolar,and bipolar TURP should be included as in-patient procedures in the cost model to reflect the setting they are routinely used in the NHS. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers and combinations of devices are needed.

Subgroups to be considered	• **High risk patients** should be considered as a subgroup due to the different resource consequences for this population. This group may include:
	  • people with pacemakers or defibrillators and those at risk of bleeding sequelae (including people on anti-coagulation therapy, with a history of bleeding disorders, an implanted prosthetic heart valve, implanted coronary stents, patients on aspirin therapy for prior coronary events, patients with prior deep vein thrombosis [DVT] or a high risk of DVT, stroke survivors, haemophiliacs, and patients who do not wish to have blood transfusions).
	  • people with a prostate size greater than 100ml
	  • people with urinary retention
	• **Settings** of the procedure should be considered as separate groups given the cost implications from this. The procedure is expected to be carried out as a day case, but a small proportion of individuals may be admitted as inpatients.	

Special considerations, including those related to equality	The condition of BPH is most common in men over the age of 50, so the GreenLight XPS laser system is primarily for use in this population. This is a function of the clinical condition for which the technology is indicated and is not likely to be considered an equalities issue. LUTS secondary to BPH are more prevalent in black men than men of white or Asian origin. This is also a function of the clinical condition, not of the technology itself. Laser vaporisation technology such as GreenLight has the potential to reduce the risk of bleeding compared with other surgical options and so may improve access to medical treatment for BPH in these previously excluded groups. These may include people on anticoagulant therapies, those with bleeding disorders and those whose beliefs prevent them from receiving blood transfusions, many of whom may be covered under the 2010 Equality Act. This technology may be appropriate for individuals who do not identify as male but have a prostate and may have BPH that requires treatment. Gender is a protected characteristic under the 2010 Equality Act. Greenlight is contraindicated for people with prostate cancer. Cancer is recognised as a disability. Disability is a protected characteristic under the 2010 Equality Act.	
Special considerations, specifically related to equality	Are there any people with a protected characteristic for whom this device has a particularly disadvantageous impact or for whom this device will have a disproportionate impact on daily living, compared with people without that protected characteristic?	No
	Are there any changes that need to be considered in the scope to eliminate unlawful discrimination and to promote equality?	No

	Is there anything specific that needs to be done now to ensure the Medical Technologies Advisory Committee will have relevant information to consider equality issues when developing guidance?	No
Any other special considerations	People who wish to preserve sexual function and fertility.	

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Information request from the sponsor for Medical Technologies Guidance review of MTG29 GreenLight XPS for treating benign prostatic hyperplasia

Review of MTG29: GreenLight XPS for treating benign prostatic hyperplasia

The original guidance was issued in June 2016.

The review date for this guidance is January 2020.

Company update

1. **Changes in the technology: MTG29 was on Greenlight XPS and and the MoXy disposable laser fibre**

    a. Is the technology still available to the NHS in the UK? **Yes**

    b. If the technology has changed, what it the latest current version and when was this model first marketed in the UK? **Please provide technical specifications which show the differences. No changes to the technology**

    c. Does the new model perform the same function and use the same mode of action as the technology in MTG29? **n/a**

    d. Does the new model have a new CE mark? **n/a**

    e. Has the cost of the technology changed since the original guidance? Please give details (this can be kept commercial-in-confidence). **No**

1. **Is the company aware of any new clinical evidence on the use of Greenlight XPS available since the original evaluation (i.e. after**

November 2015)? Yes, new evidence to support the use of Greenlight Laser in high risk patients, i.e.

- **have an increased risk of bleeding or**
- **have prostates larger than 100 mL or**
- **have urinary retention.**

If new evidence is available, please give brief details, a reference for published evidence or a title and one line description for unpublished evidence – please complete a form in appendix 1 for each piece of unpublished evidence.

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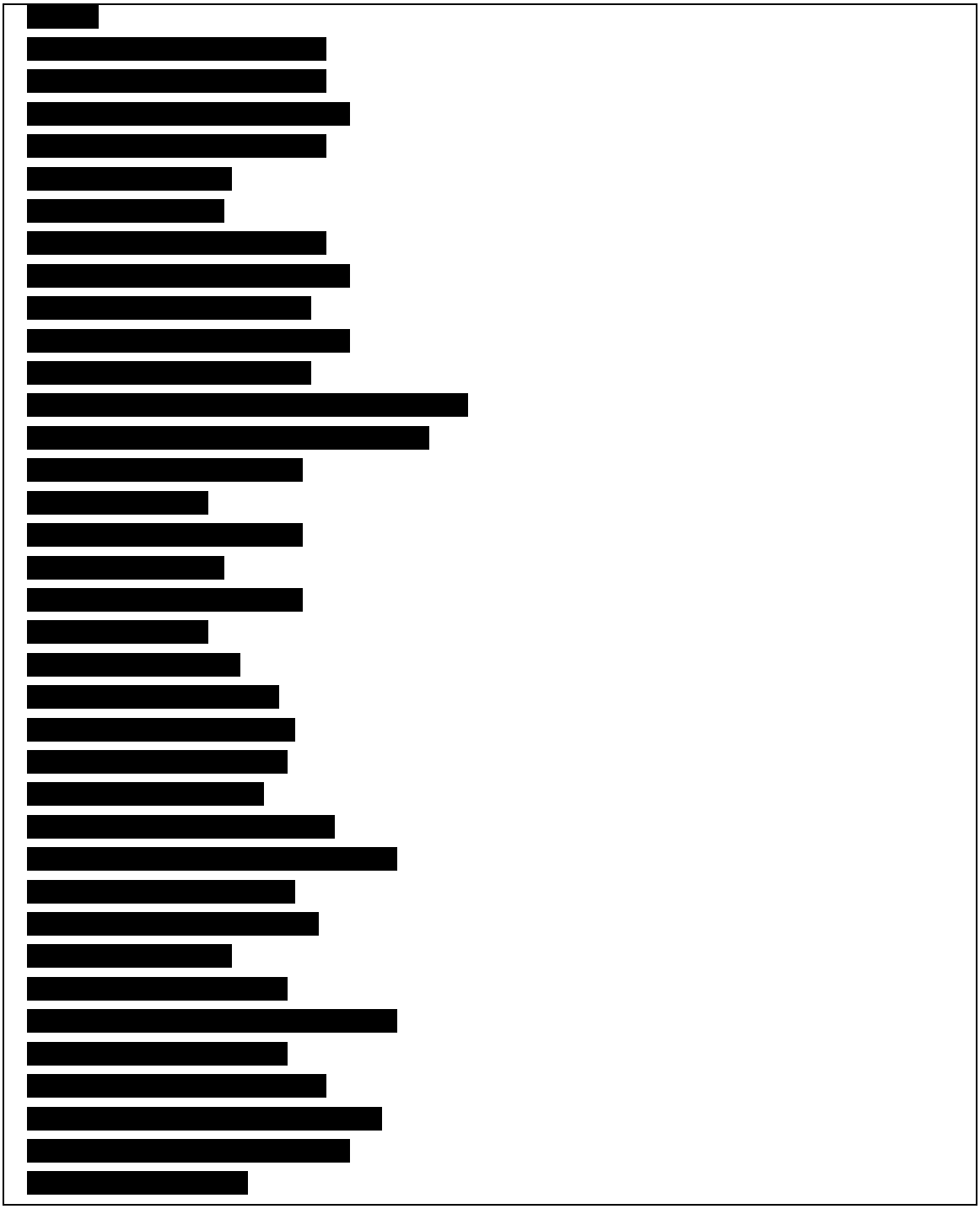
2. **Is the company aware of any adoption or usage data (such as audit) from the NHS or elsewhere?** Please give details where possible, this can be kept commercial-in-confidence as required.

No (BAUS requires that clinicians audit BPH procedures, so this information might be obtained from Urologist performing the procedure)

3. **Does the company have a list of NHS users?** If so, could you please append a list to this submission, this can be kept commercial-in-confidence as required.



4. Has the technology added new indications or is now used in new applications not covered by the original guidance? If so, please give details.

No

5. **Additional information**

Any other relevant information supporting the use of the technology.

High Risk – Increased Risk of Bleeding

There is an increasing use of oral anticoagulation agents (Warfarin and DOACs) and anti-platelet drugs within the population of men in the general population for prevention of thromboembolism, the prevention of stroke and systemic embolization in patients with non-valvular AF, in patients with mechanical valves, following acute coronary syndrome and post cardiac interventions such as stent placement. A general appraisal of the role of Warfarin and DOACs has been provided by NICE, in KTT16, with reference to multiple NICE guidance

documents that further show the increasing prevalence of anticoagulation therapy.

2014 Guidance from the American Urological Association (Culkin et.al.) reviewed the available evidence and concluded laser prostate surgery, including GreenLight XPS vaporization of the prostate to be safe in men on ongoing oral anticoagulation therapy.

Recent guidance from the European Association of Urology (Gravas et. al.) evaluates the evidence base for GreenLight laser Vaporization, including in the context of anticoagulated patients.

High Risk – Prostates Larger than 100ml

There is also further published evidence available examining the effectiveness of GreenLight XPS in treating men with larger prostates (Valdiviseo; Meskawi; Hibon; Akhtar; Lanchon; Campobasso; Thoulouzan; Ghahhar; Stone and others). Again, these are predominantly cohort studies but now constitute a growing body of literature to support the safety and efficacy of GreenLight XPS in men with large prostates, utilizing conventional vaporization. There is some additional evidence that the GreenLight XPS console can also be used to perform endoscopic anatomical enucleation (EAE) of the prostate, which in common with EAE utilisng Holmium laser or bipoloar electrosurgical energies is eminently suited for treating men with large glands (Panthier; Bajic; Yoo; Misrai; Gomez-Sancha and others).

We believe that the haemostatic properties of the GreenLight XPS system are of benefit to men with larger prostates than represented in the conventional BPH RCT literature, which generally maintain an upper size limit of 80ml.

We respectfully ask that the recent literature demonstrating safety and efficacy in men with large glands be reviewed to determine, whether the guidance could be extended to this group, often representing older men (prostate size correlates strongly with age) with additional comorbidities.

High Risk – Urinary Retention

There is some further evidence that we have identified on the use of GreenLight XPS in men with long-term urinary catheters due to chromic urinary retention. (Knoblauch; Goueli and others). Again, chronic urinary retention is associated with age and therefore comorbidity and this population is very often not included in RCTs. Whilst there is no overwhelming change in the evidence landscape here, because the population of men with long term in-dwelling catheters is older and many are found within the long-term care environment, we wonder whether there is case to be made for improved care and reduced economic burden, if these men can be made catheter free. Since this group often have additional comorbidity, necessitating OAC or DOACs, in addition to potentially having larger glands, a recommendation that GreenLight XPS can or can't be used in the context of in-dwelling catheters may lessen its availability to men who might do well and be able to be catheter free.

Declaration:

Company representative: Glyn Burt

Position: Medical Director Date: 09 November 2021

Appendix 1

Unpublished study details	
Should this study be seen as: publicly available, academic-in-confidence, commercial-in-confidence? Is there a planned publication date?	
Study details [e.g. Trial code if registered as a clinical trial, authors, title, details of funding]	
Design [e.g. was it randomised, was there a control group or comparator technology, was it a post-marketing study]	
Assigned interventions [how was the technology used, how often]	
Participants [how many people were in the study, how were they selected, which indication did they have, which setting were they in e.g. hospital, GP etc]	
Follow-up period	
Primary outcome [what was the main symptom or parameter measuring the effect of the technology]	
Secondary outcome(s) [any other symptoms, parameters measured]	
Key results – efficacy	
Key results – safety [were there any side effects or adverse events]	
Information source [e.g. webpage or link to details of the study, if available]	
Any other comments	

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National Institute for Health and Care Excellence

Collated comments table

MTG Medtech Guidance:

Expert contact details and declarations of interest:

Expert #1	ANIRUDDHA CHAKRAVARTI, CONSULTANT UROLOGICAL SURGEON, THE ROYAL WOLVERHAMPTON HOSPITALS NHS TRUST, [redacted]
	Nominated by: NICE
	DOI: Provided expert opinion on Urolift procedure
Expert #2	Marios Hadjipavlou, Consultant Urological Surgeon, Guy's & St Thomas' NHS Foundation Trust, [redacted]
	Nominated by: NICE
	DOI: none
Expert #3	Maya Harris, Consultant Urological Surgeon, South Warwickshire NHS Foundation Trust, [redacted]
	Nominated by: NICE
	DOI: none
Expert #4	Ian Pearce, Consultant Urological surgeon, Manchester University NHS Foundation Trust, [redacted]
	Nominated by: NICE
	DOI: none
Expert #5	Mr Amr Emara, Consultant Urologist, Hampshire Hospitals Foundation Trust, [redacted]
	Nominated by: company
	DOI: none
Expert #6	Gordon Muir, Consultant Urologist, King's College and London Bridge Hospitals, [redacted]
	Nominated by: NICE and company
	DOI: 2009 - present : Mentor and consultant BSCI; 2018 – present: Mentor and consultant Olympus GMBH; 2013-2019 – present: Mentor and consultant Neotract
Expert #7	Mr Feras Al Jaafari, Consultant Urologist, NHS Fife, [redacted]
	Nominated by: BAUS

	DOI: Since 2017: I have been consulted (and paid) by the manufacturer (Boston Scientific) regarding this technology. I have given talks on patient centric approach in BPH sponsored by the company. Since 2018: I am a paid proctor in this procedure. I train other urologists in performing the procedure. Since 2021: I have visitors attending my theatre lists for which preceptorship fees are paid to the department.
Expert #8	James Andrew Thomas, Consultant Urological Surgeon, CTM UHB, [redacted]
	Nominated by: NICE
	DOI: none
Expert #9	Richard Hindley, Consultant Urologist, Clinical Lead for Urology and Visiting Professor, Hampshire Hospitals NHS FT, [redacted]
	Nominated by: n/a
	DOI: From approx. 2010: I do receive ad hoc payments as a clinical advisor and proctor for Boston Scientific; I was involved with the GOLIATH trial
Expert #10	Professor Iqbal Shergill, Consultant Urological Surgeon, Wrexham Maelor Hospital, [redacted]
	Nominated by: n/a
	DOI: none
Expert #11	Sanjay Rajpal, Consultant Urologist, Sheffield Teaching Hospitals, [redacted]
	Nominated by: company
	DOI: 29/09/21 I have received payment for proctoring services from Boston Scientific (manufacturer of the GreenLight XPS)

			Response
1	Please describe your level of experience with the procedure/technology, for example: Are you familiar with the procedure/technology? Have you used it or are you currently using it? Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake? Is this procedure/technology performed/used by clinicians in specialities other than your own? – If your specialty is involved in patient selection or referral to another specialty for this procedure/technology, please indicate your experience with it.	Expert #1 yes Used it, not currently using Still used in the NHS although not as widely as before Not known to be used in specialities other than urology This is a procedure to treat BPH used by urologists	
		Expert #2 I have undergone training for this procedure, however I have never performed this myself. It is not offered in my Trust, although it is offered in a nearby hospital within our regional Network (King's College Hospital), where it has been very well established for several years. According to the recent BAUS audit, Greenlight comprises 6.1% of all bladder outflow obstruction surgical procedures (https://www.baus.org.uk/_userfiles/pages//files/professionals/research//BAUS%20Bladder%20Outflow%20Obstruction%20National%20Report%20November%202020.pdf) To the best of my knowledge, Greenlight for benign prostatic hyperplasia is only performed by urological surgeons. Selection for this procedure is decided by the urologist and the patient himself. Anaesthetic input may sometimes be required to assess for fitness (for example, if a patient is deemed by the surgeon and the anaesthetist unfit for general or spinal anaesthesia,	

		prostate artery embolization or Rezum or Urolift may be offered instead).	
		Expert #3 I am very familiar with the Green Light Laser prostatectomy and performed about 200 procedures both in NHS and private sector since learning the procedure with a proctor in 2015. I do currently use it as a part of a portfolio of the procedures I offer for BPH, which also includes TURP, Rezum and Urolift. I am aware of the other centres in the region and in the country which perform the procedure routinely. It is not performed by clinicians of other specialities. Not applicable as above.	
		Expert #4 I am familiar with the technology I have not used the technology and am not aware of how widely this is used in the UK No My specialty is involved in counselling patients and selecting patients for this procedure	
		Expert #5 - I am very familiar with Green-Light Vaporisation of prostate procedure	

		- I routinely use this technique in my daily practice for the past 10 years. - This procedure is adapted by few urology NHS centres across the UK, I think the technique safety and ease of use should qualify adopting the technique in many more centres. - I am not aware that Green-light is currently used by other specialities as routine. - I have substantial experience is using green-light PVP; both technically and on research front with previous publication of our local experience, I will be comfortable to advise on selection and referral criteria.	
		Expert #6 Subspecialist LUTS BPH surgeon, teacher, researcher	
		Expert #7 - I am very familiar with this procedure. I have been involved in >500 Greenlight laser procedures over the last few years and have run multiple hands-on training courses teaching t to trainees and fellow consultants. - I am currently using it - On the recent BAUS snapshot audit the uptake is 6.1% across the UK (although this was only	

		across one month – I suspect the uptake is over 10-15% - It is only used in urology and only to treat enlarged prostates	
		Expert #8 I have been using Greenlight laser technology since its inception in 2006. I was the Co Primary investigator in the Goliath Studies and led the initial application for NICE approval 5-6 years ago. I use the technology routinely as my primary operation for BPH in the NHS and private sector. There is a widespread use within the NHS – though it maybe patchy in some regions. no I have 15 years experience and have taught this technique across various centres in UK, Europe and the USA.	
		Expert #9 Familiar – I have been using this technology since 2005 as a Consultant having trained in its use in 2003. I have performed over 1500 cases. I am still using it regularly performing 1-2 cases per week	

		There was guidance in 2016 which I was involved with – adoption advice. It is relatively underutilised in the UK. No.	
		Expert #10 Familiar with technology. Not used it or currently using it. Aware of centres in NHS using this technology. Not used elsewhere. N/A	
		Expert #11 I am currently using this technology In addition to my centre, 4 other units in the region (Yorkshire & Humber) use this technology Uptake for this technology is increasing particularly since GIRFT recommendations and with the pressures on hospital beds and the attraction of carrying out this procedure as a day case This technology is only used in urology	
2	− Please indicate your research experience relating to this procedure (please choose one or more if relevant):	Expert #1 I have done bibliographic research on this procedure. Other (please comment)	

		Expert #2 I have had no involvement in formal research on this procedure. However, I have previously provided expert opinion on this procedure to NICE, which involved some literature research.	
		Expert #3 I have done bibliographic research on this procedure and follow any publications which appear in the relation to it.	
		Expert #4 I have had no involvement in research on this procedure.	
		Expert #5 I have done clinical research on this procedure involving patients or healthy volunteers. I have published this research.	
		Expert #6 I have done bibliographic research on this procedure. I have done research on this procedure in laboratory settings (e.g. device-related research). I have done clinical research on this procedure involving patients or healthy volunteers. I have published this research. ALL OF the above	

		Expert #7 I have published (co authored papers on this topic) Trail, M., Good, D., Clyde, D., Brodie, K., Leung, S., Simpson, H., Kata, S. G., Tsafrakidis, P., Chapman, R. A., Mitchell, I., Janjua, K., & Al Jaafari, F. (2021). Day Case GreenLight Laser Photoselective Vaporisation of the Prostate (GL-PVP): Evaluation of Outcomes from a District General Hospital Experience of 538 Cases. *Journal of Endoluminal Endourology*, *4*(3), e8-e16. https://doi.org/10.22374/jeleu.v4i3.128 Trail, M., Hindley, R. G., **Al Jaafari, F**. (2021). Contemporary surgical management of benign prostatic obstruction: does there remain a place in the toolbox for TURP? *Journal of Clinical Urology*. https://doi.org/10.1177/20514158211010646 Johnston MJ, Guillaumier S, **Al Jaafari F**, Hindley RG (2019) The Urological Stethoscope: An essential aide for the modern BPH Specialist? BJUI 2020 May;125(5):632-633 doi: 10.1111/bju.14979. Epub 2020 Jan 8.	
		Expert #8 I have done bibliographic research on this procedure. I have done clinical research on this procedure involving patients or healthy volunteers. I have published this research. (Alex Bachmann and myself were lead authors / investigators in GOLIATH study) Other (please comment)	
		Expert #9	

		I have done bibliographic research on this procedure. Yes I have done research on this procedure in laboratory settings (e.g. device-related research). No I have done clinical research on this procedure involving patients or healthy volunteers. Yes We were a centre in the GOLIATH study.	
		Expert #10 I have had no involvement in research on this procedure. Other (please comment)	
		Expert #11 I have no involvement in research on this procedure.	

Current management

3	How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design? Which of the following best describes the procedure (please choose one):	Expert #1 Used since a long time. Ablative procedure, not new, not novel approach Established practice and no longer new.	
		Expert #2 Established practice and no longer new.	
		Expert #3 Green light laser prostatectomy is innovative compared to the TURP (standard). It causes less bleeding and has easier postoperative recovery. It has been developed 10-15 years ago. Established practice and no longer new.	
		Expert #4 This represents a new technology utilised to perform a well performed procedure, as such it represents a moderate variation Established practice and no longer new.	
		Expert #5 Established practice and no longer new.	
		Expert #6 Established practice and no longer new.	
		Expert #7 Established practice and no longer new.	

		Expert #8 Safer and equally effective to TURP (Goliath data) Established practice and no longer new.	
		Expert #9 Novel – uses the unique characteristics of the greenlight wavelength to selectively vaporise vascular tissue. Established practice and no longer new. There are adaptations and new ways of using the technology – for example,it can be used to enucleate. The technique I sue predominantly is that of anatomical vapourisation – using the technology for what it was designed – photoselective vapoursation down to the prostate capsule to create a TURP like cavity but with a better safety profile.	
		Expert #10 Established practice and no longer new.	
		Expert #11 This procedure is a relatively novel approach when compared to current standard of care Established practice and no longer new.	
4	Does this procedure/technology have the potential to replace current standard care or	Expert #1 Addition to other standards of care	

	would it be used as an addition to existing standard care?	Expert #2 To be used in addition to alternative treatment options for BPH.	
		Expert #3 I think the technology should be offered as a part of the portfolio of the procedures for BPH. I use TURP if histology of prostatic tissue is important for the patient, or Rezum procedure if the patient wishes to preserve ejaculation.	
		Expert #4 Used as an optional variation in care	
		Expert #5 In a stepwise approach it can be implemented more widely to prepare for future replacing of current less safe (with higher risk of complications) standard of care.	
		Expert #6 Yes and it should	
		Expert #7 Yes- it has the potential to replace the current standard of care due to its higher safety profile	
		Expert #8 Yes – replace	
		Expert #9 Could replace – perhaps in combination with other procedures that have a better safety profile	

		than TURP such as HoLEP and the minimally invasive procedures Rezum and Urolift.	
		Expert #10 Used in addition	
		Expert #11 Potential to replace the current standard of care	

Potential patient benefits

5	Please describe the current standard of care that is used in the NHS.	Expert #1 TURP, Urolift, HoLEP, Rezum, Green light laser ablation	
		Expert #2 Several treatment options are available for management of BPH. If there is indication for surgical intervention, the options offered are: transurethral resection of the prostate (TURP – can be bipolar or monopolar), Holmium laser enucleation of Prostate (HoLEP), Urolift, Rezum, or Prostate Artery Embolization. They have a different side effect profile and they are indicated for different sizes of prostates. The options are therefore discussed and agreed with each patient.	
		Expert #3 BAUS Bladder Outlet Obstruction audit (2019) has demonstrated that TURP (both monopolar and bipolar) is the leading procedure and Green	

		Light laser prostatectomy was used in 6.1% of cases.	
		Expert #4 Current standard of care for outflow surgery is now variabl;e with multiple options being available and offered including 1. TURP 2. Bipolar TURP 3. Urolift 4. HoLEP 5. Rezum 6. Prostate artery embolisation	
		Expert #5 Transurethral resection of prostate either Monopolar or Bipolar is the current standard of care in nearly 80% of UK centres with the remaining using laser technique as supplementary.	
		Expert #6 Variable depending on local expertise and prejudices	
		Expert #7 The BAUS snapshot audit showed that TURP was used in the treatment of 60.5% of all patients requiring bladder outflow obstruction surgery.	

		Expert #8 My practice – Green light laser followed by TURIS (bipolar TURP – second choice)	
		Expert #9 The conventional standard of care has been TURP for the majority. This is no longer the case in my opinion. I am Chair of the BOO GIRFT Academy and the document we are working on is nearly complete – we feel that the new gold standard is to have a portfolio of treatment options. BAUS our national organisation are in agreement with this principle. No one procedure treats all anymore as we need to be patient centric rather.	
		Expert #10 Monopolar TURP	
		Expert #11 TURP (monopolar and bipolar) is currently the most commonly performed bladder outflow surgical procedure in the NHS	
6	Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this?	Expert #1 Aquablation	
	If so, how do these differ from the procedure/technology described in the briefing?	Expert #2 The options mentioned above form the alternatives, and they have different indications and contraindications as well as different side	

		effect profiles, which are well documented in the literature.	
		Expert #3 The competing procedures are TURP, Rezum, HOLEP, PAE, Aquablation and Urolift. All of these procedures could be used for treatment of BPH, depending on prostate volume, presence of urinary retention, patient's preference and local availability.	
		Expert #4 The alternatives are as above They employ a different mechanism TURP involves the use of heat (current) to remove prostatic tissue Urolift utilises surgical implants to compress and pin back the prostatic tissue Rezum involves injections of steam into the prostate resulting in cell death PAE involves occluding the main blood supply to the prostate resulting in cell death and shrinkage	
		Expert #5 There is more than one laser technology used in the BPH market, targeting less bleeding risk with shorter hospital stay and robust out-comes, but according to current evidence Green-Light PVP is one of the safest modalities.	

		Expert #6 HoLEP, REZUM, ITIND, Urolift All capable of outperforming TURP in terms of bed usage and recovery for selected patients in some cases. Both lasers equivalent to or better than TURP but safer.	
		Expert #7 No other vaporising technique competes with Greenlight laser from a mode of action point of view. There are other novel technologies with different mode of action that are NICE approved we lack long term data regarding durability (urolift, Rezum)	
		Expert #8 Holmium enucleation of prostate	
		Expert #9 No – Greenlight is very good for patients with a bleeding tendency and overall has a very good safety profile.	
		Expert #10 Bipolar Vaporisation – different in sense of different energy source used eg: electric current rather than laser.	
		Expert #11	

		1. Holmium laser Enucleation of Prostate (HOLEP)- this is a different type of laser which is used for the same problem. This procedure is enucleation of the prostate whereas the Greenlight laser involves photo-selective vaporisation of the prostate. HOLEP has a greater learning curve, involves overnight stay and will need additional equipment like a morcellator. HOLEP procedure is very useful for patients with large prostates (100cc+) 2. Transurethral vaporisation of the prostate (TUVP) : This technology results in electro-vaporisation of the prostate. A modification of the loop in TURP is used and the prostate tissue is treated resulting in a cavity similar to TURP and GLLP 3. Thullium Laser vaporesection of prostate (ThuVARP) : Thullium laser can be used to remove the obstruction in the prostatic urethra using principles of vaporisation and nucleation. Currently available in a very few centres in the UK. Non-inferiority to TURP has been shown in studies.	
7	What do you consider to be the potential benefits to patients from using this procedure/technology?.	Expert #1 Choice of an alternative procedure towards surgical treatment of bladder outflow obstruction	
		Expert #2 The main advantages of this technology over other BPH procedures such as TURP, is the haemostatic property of laser, which means that an anticoagulated patient may not need to stop their medication for the operation. Also this procedure can be performed as day surgery, as	

		opposed to TURP or HoLEP which typically require 1-2 nights inpatient stay. It is also considered a less difficult procedure to learn compared to alternatives such as HoLEP or possibly TURP.	
		Expert #3 The benefits of Green Light laser include reduced bleeding and need for postoperative bladder irrigation with subsequent earlier discharge and easier postoperative recovery.	
		Expert #4 Lower blood loss compared to standard TURP Fewer complications Shorter hospital stay	
		Expert #5 Safe / less risk of bleeding/ no TUR syndrome risk - and accordingly risk of re-hospitalisation and need for blood-transfusion will be significantly less compared to standard technique – eventually leading to overall less hospital nights.	
		Expert #6 Faster recovery better use of resources	
		Expert #7 Higher safety profile than TURP. Can be performed as a true daycase. Less bleeding. Shorter surgical time. Long term data available in the literature.	

		Expert #8 Safety / day case procedure / return to normal health quicker than the standard of care in NHS	
		Expert #9 Good safetry profile / reduced risk of bleeding/ no TUR syndrome risk - and accordingly risk of re-hospitalisation and need for blood-transfusion will be significantly less compared to standard technique. A reliable daycase procedure. No requirement for any irrigation post procedure in 99%.	
		Expert #10 Less bleeding risk and hence can be potentially used as daycase surgery especially in patients on anti-coagulants which are high risk patients.	
		Expert #11 1. Less blood loss- safer in patients on anti-platelet and anticoagulant medications and the general population as there will be less physiological strain 2. Reduced risk of secondary haemorrhage – resulting in less use of healthcare resources post-operatively (as the laser is very haemostatic) 3. Can be done as day case 4. Similar outcomes to TURP	

Potential system impact

8	Are there any groups of patients who would particularly benefit from using this procedure/technology?	Expert #1 Patients needing a short procedure with ablative therapy to treat bladder outflow obstruction from a small to medium sized prostatic adenoma with no need for histological analysis of tissue	
		Expert #2 As mentioned above, patients on anticoagulants that is best to avoid stopping may be more suitable for Greenlight PVP than any of the other options.	
		Expert #3 Elderly patients, especially on anticoagulation	
		Expert #4 Men with symptoms from bladder outflow obstruction caused by prostatic enlargement who wich a more long term proven surgical rsolution	
		Expert #5 Older patients and patients with higher risk of bleeding or on anti-coagulation. And this is the wider range of patients requiring this procedure.	
		Expert #6 High risk, anticoagulated, patients with implantable devices, patients who enjoy sex	
		Expert #7	

		High risk patients – catheterised, on anticoagulants, co-morbid (ASA III, IV)	
		Expert #8 Elderly / those anti-coagualted / larger prostate volumes	
		Expert #9 Older patients and patients with higher risk of bleeding or on anti-coagulation.	
		Expert #10 As above	
		Expert #11 1. Patients who are on anticoagulants/ anti-platelets agents 2. Most patients who need a TURP might be benefitted by this	
9	Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system? Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?	Expert #1 I do not think so No	
		Expert #2 This procedure can be performed as day surgery, as opposed to TURP or HoLEP. The functional outcomes are comparable with that of TURP, which is slightly more invasive with a higher risk of bleeding perioperatively, although not very significant nowadays with bipolar TURP.	
		Expert #3	

		It does lead to the reduced hospital stay, less invasive treatment, less need for postoperative blood transfusion, easier recovery with less visits.	
		Expert #4 Shorter hospital stay	
		Expert #5 Yes, less risk or re-hospitalisation, less burden on blood banks (hardly any requirement for blood transfusion with no need for routine group & save), many cases can be a day case procedure and eventually shorter hospitalisation.	
		Expert #6 Potential to abolish over 90% of overnight stays for men with LUTS BPH including urinary retention	
		Expert #7 Yes, especially in the peri/post-COVID recovery era. Patients will not require an inpatient bed as they can be done as a true daycase. If the patient gets admitted, they are usually discharged the following morning. This is crucial given the bed pressures in the NHS. The functional outcomes are equivalent to TURP in the long term.	
		Expert #8 It has already in my practice Yes and yes	

		Expert #9 Yes, no inpatient bed required. Reduced bleeding risk. Good procedure for those with higher ASA scores. Yes	
		Expert #10 Potentially less hospital stay. Functional outcomes likely to be similar though.	
		Expert #11 Yes – in my centre, we were doing TURP previously with average length of stay being 3.2 days. Since starting Green light laser in 2018, 62% of these patients are done as day case. The remaining 38% patients stay in overnight mainly due to social, general frailty reasons. Outcomes studies so far suggested-1. Reduced LOS 2. Efficacy similar to TURP 3.Reduced re-admission rates with post op complications. It is a less invasive treatment compared to TURP	
10	Considering the care pathway as a whole, including initial capital and possible future costs avoided, is the procedure/technology likely to cost more or less than current standard care, or about the same? (in terms of staff, equipment, care setting etc)	Expert #1 About the same	
		Expert #2 I am not aware of the financial aspects around Greenlight.	

		Expert #3 I think the cost is similar to TURP.	
		Expert #4 Probably less	
		Expert #5 Overall factoring the re-hospitalisation and inpatients nights. this proven to be a cost-effective procedure compared to current standard of care.	
		Expert #6 A bit less	
		Expert #7 • Yes, the procedure will have potential cost savings • As per the NICE document in 2016 - “NICE's resource impact report estimates that the annual cost saving for the NHS in England is around £2.3 million. In a plausible scenario of 70% of treatments being done as day cases, the cost saving may be up to £3.2 million.”	
		Expert #8 Last nice assessment – from memory – if greenlight replaced every TURP in nHS – save £167 per case	
		Expert #9	

		Less by £500 approx when compared to TURP as per previous data.	
		Expert #10 More costly, as laser fibres will be more expensive than loops used in monopolar TURP.	
		Expert #11 This procedure should cost less (or cost equal) than the current standard of care	
11	What do you consider to be the resource impact from adopting this procedure/technology (is it likely to cost more or less than standard care, or about same-in terms of staff, equipment, and care setting)?	Expert #1 Cost of fibres could be balanced by shorter length of stay	
		Expert #2 I am unable to comment on cost-related questions. In terms of equipment, this technology requires on a capital investment on the laser device/generator and then consumables. It also required to be performed in laser-safe theatres (which may require specific installations), a high energy socket, and theatre staff laser and procedure-specific training.	
		Expert #3 I think it is cost-neutral with higher outlay for the laser fibre and reduced costs due to reduced hospital stay and less intensive nursing required.	
		Expert #4 High initial cost for the equipment On going costs re maintenance contracts	

		Expert #5 As expected, there will be initial capital investment to introduce the service, but this will be automatically diluted with less inpatient nights and less risk of post-operative complications with no need for transfusion or using critical care beds.	
		Expert #6 A bit less	
		Expert #7 Cost saving Safer procedure/ less bleeding Shorter hospital stay Shorter surgical time	
		Expert #8 You need to buy new equipment initially- laser and adapt your rsectoscopes	
		Expert #9 Less than standard of care. The cost of a TWOC is more than off set by the absence of a requirement for blood transfusion, reduced bed stay and lower risk of side effects requiring treatment such as ED and strictures.	
		Expert #10 Similar resources.	
		Expert #11	

		This procedure should cost less (or cost equal) than the current standard of care	
12	What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?	Expert #1 Laser safe theatre	
		Expert #2 Laser-safe theatre (e.g. laser curtains, laser-stafety goggles, etc) and laser-certified theatre staff.	
		Expert #3 Laser machine (with fibres and glasses), laser-safe theatre, staff training	
		Expert #4 Laser training Protective eye wear	
		Expert #5 Laser safe operating theatre with the relative personnel training are required for using this technology	
		Expert #6 none	
		Expert #7 Laser proofing of the operating theatre (most urology theatres are laser proofed). The purchase of the laser machine (the company can place it otherwise on a fibre consumption contract). Staff need to be trained.	

		Expert #8 Anaesthesia – GA or spinal and. A day case theatre	
		Expert #9 Laser safe theatre.	
		Expert #10 Laser compatible theatres. Laser trained staff.	
		Expert #11 1. Theatres: should be made laser safe as per standard guidelines. 2. Power socket for laser will be needed 3. Equipment : Minor change to the existing TURP kit will be needed like the beak of the sheath will need changing to metal beak and a separate laser bridge will need to be procured 4. Laser safety glasses 5. Capacity for day case surgery and post procedure clinic slots for catheter removal will need to be factored in 6. Surgeon and theatre staff training	

General advice

13	Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?	Expert #1 Staff needs laser safety training, operator needs to be trained, surgeon needs training to do the procedure	
		Expert #2 Yes – laser safety certification, as well as training specific to the use of this device. These can usually be arranged and organised by the company.	
		Expert #3 Laser training for the staff with the dedicated laser operator in the theatre during the procedure.	
		Expert #4 Yes, lasewr safety training for all staff	
		Expert #5 Yes – The standard laser safety course is mandatory requirement plus the expected technique training that is currently provided through the relative courses or in many centres as part of specialty training program.	
		Expert #6 Validated simulator and mentorship programmes exist	
		Expert #7	

		Core laser knowledge course and basic laser handling training (transferrable from other existing laser knowledge skills).	
		Expert #8 Yes	
		Expert #9 Yes – training as per company standard which includes simulator training and proctoring of initial cases.	
		Expert #10 As above.	
		Expert #11 Yes- Laser safety course (run by the manufacturer), simulator training and hand on training with a proctor (provided and supported by the manufacturer)	

Other considerations

14	What are the potential harms of the procedure/technology? Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence: Adverse events reported in the literature (if possible, please cite literature)	Expert #1 No histology available Powerful laser - needs to be handled with care by adequately trained staff	

	Anecdotal adverse events (known from experience) Theoretical adverse events	Bleeding, secondary haemorrhage	
		Expert #2 This technology has been well tested over several years and is generally considered a safe procedure, when performed by appropriately trained staff. The XPS (180W) should be evaluated separately from the older model (120W) which was less powerful, therefore considered slower and less effective and appropriate for very large prostate glands. Anecdotally, I have heard from colleagues that a significant proportion of patients will suffer from dysuria, urethral discomfort, urgency and frequency, due to sloughing of the tissue from the prostatic cavity (when compared to the other BPH treatment options). However, although relatively common, this is not considered a major side effect and usually improves with time or with the use of non-steroidal anti-inflammatory drugs. Injury to the ureteric orifices by the laser has also been reported, which can lead to severe complications requiring surgical intervention (ureteric strictures). As with most BPH procedures (except perhaps HoLEP), there is prostate regrowth over years and there is therefore a reintervention rate associated with Greenlight.	
		Expert #3 The authors below quote bladder neck stenosis in 1%, but also I counsel the patients preoperatively that the procedure could cause haematuria, infection (UTI), retrograde	

		ejaculation in the majority of cases, incontinence (serious in about 1%), erectile difficulties.	
		Expert #4 Recurrence Stricture Erectile dysfunction	
		Expert #5 As any Laser technology, respecting the standard safety requirement will keep it safe to use. Using the necessary protective equipment and having a laser officer in theatre is mandatory part of using this technology to keep it safe. Adverse events: bleeding necessitating transfusion (<1%) - Retrograde ejaculation (50-60%), risk of infection (2 -5%), Risk of scarring (urethral stricture/ Bladder neck stenosis – 1-2%) - Need for re-do (3-7%) - Incontinence (<1%)	
		Expert #6 As with all LUTS BPH porcedures, but less common	
		Expert #7 Any surgical procedure carries some risks – Bleeding – requiring transfusion <1% Stricture – 2-5% Retreatment – up to 10-15% in 10 years	

		Impotence <1% Retrograde ejaculation 50-70%	
		Expert #8 Sane as TURP – uti / bladder neck scarring UTI – 5%, retrograde ejaculation 66% / bleeding – rare <1% n/a n/a – just read the papers from Goliath papers – top quality studies – answers all these questions	
		Expert #9 Reduced complication rates when compared with TURP (GOLIATH Trial). ED 1-2% dry ejaculation 30-50% Incontinence < 1% Transfusion 0%	
		Expert #10 Potentially high rates of patients needing re-do surgery in future.	
		Expert #11 Procedure specific: Dysuria, Urinary tract Infection, Sepsis, Bleeding (risk of transfusion<1%), Retrograde ejaculation (70-90%), Impotence(1-2%), Transient incontinence (5%), Bladder neck stenosis (5%), urethral	

		stenosis (1-5%), Adjacent organ injury(ureteric/ bladder injury)<1%, No tissue for histology, Failure to void, Re-operation rate (slightly higher than TURP) Risks from anaesthesia and hospitalisation including DVT, PE From experience: Sepsis necessitating ITU stay and further complicated by leg ischaemia needing embolectomy, cardiac arrest intra-operatively followed by subsequent demise, dystrophic calcification (in patients (x3) who had previous prostate radiotherapy) necessitating trans-urethral resection of the calcification in the prostatic urethra	
15	Please list the key efficacy outcomes for this procedure/technology?	Expert #1 Persistent relief of symptoms in a safe and effective way with minimal complications	
		Expert #2 Perioperative – inpatient stay / intraoperative complications / successful trial without catheter Long-term – catheter-free rate / IPSS score / reintervention rate	
		Expert #3 Mean IPSS nadir was reached at three years, with a drop of 80.4% (−21.1 points). Similarly, mean quality of life (QoL) score dropped by 82.8% after three years (preoperative mean of 4.7). With respect to mean Qmax, there was an increase by 72.7% (+14.7 mL/s) at one year, reaching the value of 19.9 mL/s. Moreover,	

		mean PVR was 32.8 mL at four years compared to 345 mL preoperatively. [Kevin C. Zorn et all. Photoselective vaporization of the prostate with the 180-W XPS-Greenlight laser: Five-year experience of safety, efficiency, and functional outcomes. Can Urol Assoc J. 2018 Jul; 12(7): E318–E324.]	
		Expert #4 IPSS score Complication rate Length of stay Reoperation rate	
		Expert #5 Safely managing bladder outlet obstruction symptoms and urinary retention with significantly improve in patient's quality of life.,	
		Expert #6 IPSS scores, catheter free retention outcomes	
		Expert #7 Improvement in flow, post void residual, IPSS score, QoL scores and successful trials without catheter (for catheterised patients)	
		Expert #8 Improvement in IPSS, Qol, QMax on a flow rate / catheter free rate if patient is in retention	
		Expert #9	

		2-5 year retreatment rates, PROMS's, complication rates	
		Expert #10 Symptom improvement during clinical follow up – measured with IPSS.	
		Expert #11 1. Improvement in IPSS scores and Qmax 2. Day case rates 3. Successful TWOC rates in patient treated for urinary retention 4. Re-operation rates (long term-i.e.>36 months)	
16	Please list any uncertainties or concerns about the efficacy and safety of this procedure/?	Expert #1 Risk of sexual dysfunction and incontinence. No tissue available for histological analysis.	
		Expert #2 As involves laser, needs to be performed by competent or well-supervised staff to minimise laser-associated risks to patient and staff (very rare).	
		Expert #3 There is an uncertainty regarding the durability of the outcome after green light laser prostatectomy and also whether it adds value compared to the bipolar TURP, which cases less bleeding that the traditional monopolar TURP and does not have risk of TURP syndrome.	
		Expert #4	

		NA	
		Expert #5 NA	
		Expert #6 n/a	
		Expert #7 Uncertainties regarding its efficiency for prostates over 150g (very big).	
		Expert #8 No concerns if surgeons are well trained	
		Expert #9 N/A	
		Expert #10 Potentially high rates of patients needing re-do surgery in future	
		Expert #11 1. Long term follow up data	
17	Is there controversy, or important uncertainty, about any aspect of the procedure/technology?	Expert #1 As above regarding tissue diagnosis.	
		Expert #2 Not that I am aware of.	
		Expert #3	

		As above	
		Expert #4 NA	
		Expert #5 NA	
		Expert #6 n/a	
		Expert #7 -	
		Expert #8 No	
		Expert #9 N/A	
		Expert #10 Potentially high rates of patients needing re-do surgery in future	
		Expert #11 Not that I am aware of	
18	If it is safe and efficacious, in your opinion, will this procedure be carried out in (please choose one):	Expert #1 Most or all district general hospitals.	
		Expert #2 Most or all district general hospitals.	

		Expert #3 Cannot predict at present.	
		Expert #4 Cannot predict at present.	
		Expert #5 Most if not all NHS hospitals.	
		Expert #6 Most or all district general hospitals. BUT BPH care should be concentrated in regional hubs for best outcomes and efficiency	
		Expert #7 Most or all district general hospitals.	
		Expert #8 Most or all district general hospitals.	
		Expert #9 Most or all district general hospitals.	
		Expert #10 Most or all district general hospitals.	
		Expert #11 Most or all district general hospitals.	
19	Please list any abstracts or conference proceedings that you are aware of that have	Expert #1 http://dx.doi.org/10.1136/bmjopen-2018-028855	

	been recently presented / published on this procedure/technology (this can include your own work). Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.	Expert #2 Haudebert C. PT322 Diabeted may compromise the functional outcomes of Greenlight laser XPS-180W photoselective vaporization of the prostate. European Association of Urology Congress July 2020. Chavarriaga Soto J. P0083 Outpatient 180 W XPS GreenLight Laser photoselective vapolization of the prostate: Seven year experience. European Association of Urology Congress 2021 Reale GFM. PT316 Surgical performance of greenlight laser therapy for benign prostatic hyperplasia: preliminary results in terms of operative profile, safety and functional outcomes from a retrospective multicentre Italian database study. European Association of Urology Congress July 2020. Ghobrial FK. P0088 Greenlight (532nm) laser transurethral prostatectomy for treatment of benign prostate obstruction using XPS-180Watt system, does it pass the test of time? European Association of Urology Congress 2021 Ibrahim A. P0086 GreenLight Laser prostatectomy: are outcomes sustainable after a decade of surgery? A single center experience with up to 15 years' followup. European Association of Urology Congress 2021	

		Expert #3 I think NICE should be aware of BAUS BOO audit, the results of which have been presented at BAUS 2021 and are about to be published formally.	
		Expert #4 NA	
		Expert #5 I selected some landmark reviews (meta-analysis / GOLIATH randomised study) 1. Lai S, Peng P, Diao T, Hou H, Wang X, Zhang W, Liu M, Zhang Y, Seery S, Wang J. Comparison of photoselective green light laser vaporisation versus traditional transurethral resection for benign prostate hyperplasia: an updated systematic review and meta-analysis of randomised controlled trials and prospective studies. BMJ Open. 2019 Aug 21;9(8):e028855. doi: 10.1136/bmjopen-2018-028855. PMID: 31439603; PMCID: PMC6707662. 2. Thomas JA, Tubaro A, Barber N, d'Ancona F, Muir G, Witzsch U, Grimm MO, Benejam J, Stolzenburg JU, Riddick A, Pahernik S, Roelink H, Ameye F, Saussine C, Bruyère F, Loidl W, Larner T, Gogoi NK, Hindley R, Muschter R, Thorpe A, Shrotri N, Graham S, Hamann M, Miller K, Schostak M, Capitán C, Knispel H, Bachmann A. A Multicenter Randomized Noninferiority Trial Comparing GreenLight-XPS Laser	

		Vaporization of the Prostate and Transurethral Resection of the Prostate for the Treatment of Benign Prostatic Obstruction: Two-yr Outcomes of the GOLIATH Study. Eur Urol. 2016 Jan;69(1):94-102. doi: 10.1016/j.eururo.2015.07.054. Epub 2015 Aug 15. PMID: 26283011. 3. Elshal AM, Elkoushy MA, El-Nahas AR, Shoma AM, Nabeeh A, Carrier S, Elhilali MM. GreenLight™ laser (XPS) photoselective vapo-enucleation versus holmium laser enucleation of the prostate for the treatment of symptomatic benign prostatic hyperplasia: a randomized controlled study. J Urol. 2015 Mar;193(3):927-34. doi: 10.1016/j.juro.2014.09.097. Epub 2014 Sep 28. PMID: 25261801. 4. Corbel L, Della Negra E, Berquet G, Codet YP, Boulière F, Braguet R, Trifard F. Vaporisation laser prostatique par GreenLight (180 W) en ambulatoire: évaluation prospective sur 115 patients [Ambulatory prostate photoselective vaporisation with GreenLight laser (180W): prospective evaluation from 115 patients]. Prog Urol. 2014 Oct;24(12):733-7. French. doi: 10.1016/j.purol.2014.08.238. Epub 2014 Sep 17. PMID: 25241244.	
		Expert #6 Hundreds of papers	

		Expert #7 Recent work – Trail, M., Good, D., Clyde, D., Brodie, K., Leung, S., Simpson, H., Kata, S. G., Tsafrakidis, P., Chapman, R. A., Mitchell, I., Janjua, K., & Al Jaafari, F. (2021). Day Case GreenLight Laser Photoselective Vaporisation of the Prostate (GL-PVP): Evaluation of Outcomes from a District General Hospital Experience of 538 Cases. *Journal of Endoluminal Endourology*, *4*(3), e8-e16. https://doi.org/10.22374/jeleu.v4i3.128 Abolazm AE, El-Hefnawy AS, Laymon M, Shehab-El-Din AB, Elshal AM. Ejaculatory Hood Sparing versus Standard Laser Photoselective Vaporization of the Prostate: Sexual and Urodynamic Assessment through a Double Blinded, Randomized Trial. J Urol. 2020 Apr;203(4):792-801. doi: 10.1097/JU.0000000000000685. Epub 2019 Nov 25. PMID: 31763948. Campobasso D, Ferrari G, Frattini A. Greenlight laser: a laser for every prostate and every urologist. World J Urol. 2020 Oct 26. doi: 10.1007/s00345-020-03499-z. Epub ahead of print. PMID: 33104906. Stone BV, Chughtai B, Kaplan SA, Te AE, Lee RK. GreenLight laser for prostates over 100 ml: what is the evidence? Curr Opin Urol. 2016 Jan;26(1):28-34. doi: 10.1097/MOU.0000000000000237. PMID: 26626882.	

		Expert #8 I have presented > 10 abstracts myself at various meetings internationally. Read the publications from Goliath	
		Expert #9 Comparative Study Arch Ital Urol Androl 2020 Oct 1;92(3). doi: 10.4081/aiua.2020.3.169. Comparison of GreenLight 180-W XPS laser vaporization versus transurethral resection of the prostate: Outcomes of a single regional center Daniele Mattevi 1 , Lorenzo Luciani, Rosa Spina, Claudio Divan, Stefania Cicuto, Tommaso Cai, Valentino Vattovani, Marco Puglisi, Stefano Chiodini, Gianni Malossini A European multicenter randomized noninferiority trial comparing 180 W GreenLight XPS laser vaporization and transurethral resection of the prostate for the treatment of benign prostatic obstruction: 12-month results of the GOLIATH study. J Urol. 2015 Feb;193(2):570-8. doi: 10.1016/j.juro.2014.09.001. Epub 2014 Sep 16. PMID: 25219699 Clinical Trial. Bachmann A, Tubaro A, Barber N, d'Ancona F, Muir G, Witzsch U, Grimm MO, Benejam J, Stolzenburg JU, Riddick A, Pahernik S, Roelink H, Ameye F, Saussine C, Bruyère F, Loidl W,	

		Larner T, Gogoi NK, Hindley R, Muschter R, Thorpe A, Shrotri N, Graham S, Hamann M, Miller K, Schostak M, Capitán C, Knispel H, Thomas JA.	
		Expert #10 N/A	
		Expert #11 I am not aware of any recent abstract or conference proceedings	
20	Are there any major trials or registries of this procedure/technology currently in progress? If so, please list.	Expert #1 Not to my current knowledge	
		Expert #2 Not that I am aware of	
		Expert #3 Not aware	
		Expert #4 ?	
		Expert #5 NA	
		Expert #6 No	
		Expert #7 n/a	

		Expert #8 Goliath study	
		Expert #9 Not that I am aware of – other than a study in France looking at the safety of the procedure in patients with a bleeding tendency.	
		Expert #10 N/A	
		Expert #11 I am in the process of setting up a region wide registry (Yorkshire & Humber) Depending on how this evolves, I am in talks with users in other regions for collaboration on a nation-wide registry for all Greenlight users	
21	Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?	Expert #1 20% of target population	
		Expert #2 According to the BAUS national audit, approximately 1620 BPH procedures were performed in a year. I estimate ~80% of those would be eligible for this technology.	
		Expert #3 I think about a half of the target population of men with BPH seeking surgical treatment would be suitable for the technology.	
		Expert #4	

		Currently approx 25,000 patient per year are suitable but only a minority of these patients will end up having this technology through a mixture of restricted availability and newer less invasive options	
		Expert #5 Between 40-50 % of target population.	
		Expert #6 20k/year	
		Expert #7 I would suspect that atleast 60-70% of patients with bladder outflow obstruction would be eligible for thus procedure.	
		Expert #8 UK 10,000	
		Expert #9 25-40% - approx. 4000-5000	
		Expert #10 Potentially 70-75% of target population.	
		Expert #11 In my opinion- most patients who need a TURP would be eligible for this procedure Around 25,000 bladder outflow surgeries are carried out annually in the UK. Based on the BAUS National Snapshot Audit data, currently GLL is offered to around 10% of all patients. This might increase with the GIRFT	

		recommendations. So around 2500-3000 procedures based on the current available data.	

22	Are there any issues with the usability or practical aspects of the procedure/technology?	Expert#1 Cost, training	
		Expert#2 None, beyond comments mentioned previously.	
		Expert#3 The surgeon requires training with a proctor to perform the procedure safely and effectively. It is not routinely provided in the registrar training programmes to my knowledge, whereas TURP is one of the indicative training procedures.	
		Expert #4 NA	
		Expert #5 NA	
		Expert #6 no	
		Expert #7 no	
		Expert #8 No	
		Expert #9	

		No	
		Expert #10 Teaching and training – but plenty of mentors available in UK. Availibilty of laser machine iis biggest hurdle due to cost, in current pandemic situation.	
		Expert #11 1. Capital costs (purchase or hire) & individual laser fibre costs 2. Initial training costs (short learning curve compared to other procedures) 3. Theatre time: takes between 10-20% longer time over TURP	
23	Are you aware of any issues which would prevent (or have prevented) this procedure/technology being adopted in your organisation or across the wider NHS?	Expert#1 Cost, training, no tissue diagnosis	
		Expert#2 No	
		Expert#3 Training of the surgeon and the staff, as well as availability of the technology, although I am aware that the laser is placed on pay per fibre basis by the company.	
		Expert #4 Less invasive technologies eg Rezum and Urolift which can be administered and performed in an out patient setting under LA	
		Expert #5	

		NA	
		Expert #6 Poor previous training and standardisatoin	
		Expert #7 no	
		Expert #8 No	
		Expert #9 No	
		Expert #10 Perceived lack of efficacy long term and cost of initial purchase.	
		Expert #11 1. The negative experience from the 80W Greenlight laser is likely to have affected the opinion of clinicians- the 80w laser was marketed heavily, with little training and mentorship. Also the volume clearance was sub-optimal, leading to higher rate of secondary interventions. The immediate post-operative period was also associated with dysuria and prostatitis. The above issues have been addressed by device development and subsequent evidence showing that the side effect profile has improved	

		2. Costs of adopting the new technology	
24	Is there any research that you feel would be needed to address uncertainties in the evidence base?	Expert#1 No	
		Expert#2 None specific to this technology	
		Expert#3 Randomised comparison to bipolar TURP and other technologies (HOLEP, PAE, Rezum and Urolift)	
		Expert #4 NA	
		Expert #5 NA	
		Expert #6 Impossible to run RCT's of high risk patients as standard of care (TURP) may be unethical	
		Expert #7 Further research for the efficacy of the procedure for the vey large glands.	
		Expert #8 No	
		Expert #9	

		Perhaps a study looking at bleeding risk with this approach – data should be available soon see below: Stop or Ongoing Oral Anticoagulation in Patients Undergoing PVP (SOAP) (SOAP) – underway in France study commenced 2017. V Misrai et al	
		Expert #10 Comparison trials vs other Daycase surgery treatments for BPH – eg: Rezum and Urolift. Understanding benefit of this current treatment in high risk (anticoagulated) patients.	
		Expert #11 1. Long term data on outcomes is lacking 2. Data in the NHS settings on outcomes in high risk groups like urinary retention	
25	Please suggest potential audit criteria for this procedure/technology. If known, please describe: − Beneficial outcome measures. These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured. − Adverse outcome measures. These should include early and late complications. Please state the post procedure timescales over which these should be measured	Expert#1 Beneficial outcome measures: Assess symptom improvement with IPSS and uroflowmetry Assess reintervention rate Assess complication rate Adverse outcome measures: Continence Failure to improve symptoms Reintervention rate less than 10 years	

		Expert#2 See point 15 above.	
		Expert#3 Beneficial outcome measures: - Flow rate, IPSS and quality of life after 3 months and 5 years - Hospital stay Adverse outcome measures: - Rate and type of postoperative complications over 5 years - Secondary procedures over 5 years Early complications include - Bleeding - Postoperative retention - Infection and urosepsis - dysuria Late complications include - stricture - prostatic regrowth - erectile dysfunction - incontinence - retrograde ejaculation	
		Expert #4 Beneficial outcome measures: IPSS Length of stay	

		Adverse outcome measures: Complications Reoperation rate Transfusion rates	
		Expert #5 Beneficial outcome measures: PROMS/Successful TWOC / Flow Test/ Bladder scan/Hospital stay Adverse outcome measures: Bleeding / re-hospitalisation/ persistent symptoms/ failed treatment / general complications (DVT/PE/Infection/sepsis)/Incontinence	
		Expert #6 Beneficial outcome measures: Adverse outcome measures:	
		Expert #7 Beneficial outcome measures: Age, ASA score, comorbidities, prostate volume, IPSS, post void residual, flow rate, QoL score, IIEF-2 score, ejaculation (yes/no). Successful Trial without catheter. Days of hospitalisation (True day case vs 23hr stay vs inpatient).	

		Ideally all patients should be reviewed at 3-4 months post op with identical comparators (pre-vs post op) Adverse outcome measures Retreatment rates in the first year. Strictures rate in the first 1 year. Failed Trial without catheter post treatment. Bleeding requiring transfusion during the same admission). Readmission within 1 month.	
		Expert #8 Beneficial outcome measures: Adverse outcome measures:	
		Expert #9 Beneficial outcome measures: PROM's at 3-6 months for early outcome and then 2 years for audit Satisfaction scores – would they recommend yes or no etc Adverse outcome measures: TWOC rates / 30 day readmission rates / retreatment rates in the first 1-2 years	
		Expert #10	

		Beneficial outcome measures: IPSS, SHIM scores and QOL scores during follow up (according to clinical protocols). Adverse outcome measures: Need for re-intervention with same or different treatment modality for BPH.	
		Expert #11 Beneficial outcome measures: Audit should cover long term data (>36 months) 1. IPSS and Qmax improvements 2. Day case rates 3. Successful TWOC rates (along with timing of TWOC) in patient with urinary retention 4. Re-operation / Secondary intervention rates 5. Outcomes in patients on anticoagulants/ anti-platelets agents and the elderly Adverse outcome measures: 1. Infection and sepsis rates (Early complication- upto 12 months) 2. Erectile dysfunction (Early complication- upto 12 months) 3. Storage LUTS (Early complication –upto 12 months) 4. Re-operation/ Secondary intervention rates (long term >36 months)	

26	Please add any further comments on your particular experiences or knowledge of the procedure/technology	Expert#1 n/a	
		Expert# 2 Generally, from colleagues that have been regularly using this technology, there has been good experience in terms of its safety and efficacy. In my specialist practice of BPH, I have encountered patients that have previously had Greenlight laser PVP and require further BPH surgery because of prostatic regrowth after several years. However, reintervention is a known fact for clinicians and well-counselled patients, although this is overcome by enucleated techniques such as HoLEP which have an exceptionally low reintervention rate.	
		Expert#3 n/a	
		Expert #4 NA	
		Expert #5 n/a	
		Expert #6 n/a	
		Expert #7 In my experience I believe that Greenlight laser is a safe operation and can be offered to high risk patients given its safety profile in comparison to TURP. Most frail patients can be	

		optimised by the anaesthetic/medical teams to allow for their operation to take place. This operation will be particularly useful in the COVID recovery era given the convincing long term outcomes.	
		Expert #8 I regard myself as an expert in the procedure.	
		Expert #9 It is a very reliable procedure. Bleeding is seldom a problem.	
		Expert #10 n/a	
		Expert #11 My experience 1. As a Senior Clinical Fellow at Stepping Hill Hospital, I have used the 80w Greenlight Laser (after appropriate training and mentoring in the unit) and independently performed close to 50 procedures 2. As Consultant Urologist at Sheffield Teaching Hospital- I underwent training and mentorship for the 180w Greenlight laser in 2018. I set up the laser service along with my colleague Mr Patrick Cutinha and to date have performed >250 procedures 3. I run the BPH training course- dry and wet lab (cadaveric) for the urology trainees in Yorkshire and Humber	

		4. I have been recognised as a trainer and proctor by the manufacturer (Boston Scientific) and involved in proctorship of Consultant colleagues in the UK since Sep 2021.	

NICE National Institute for Health and Care Excellence

External Assessment Centre correspondence log

GID-MT564 GreenLight XPS

The purpose of this log is to show where the External Assessment Centre relied in their assessment of the topic on information or evidence not included in the company's original submission. This is normally where the External Assessment Centre:

a) become aware of additional relevant evidence not submitted by the company;
b) needs to check "real world" assumptions with NICE's expert advisers, or;
c) needs to ask the company for additional information or data not included in the original submission, or;
d) needs to correspond with an organisation or individual outside of NICE

These events are recorded in the table to ensure that all information relevant to the assessment of the topic is captured. The table is shared with the NICE medical technologies advisory committee (MTAC) as part of the committee documentation, and is published on the NICE website at public consultation.

#	Date	Who / Purpose	Question/request	Response received
1.	24/11/2021	Query to the Company from the EAC via NICE (in advance of the Company meeting where NICE formally introduce the Company to the EAC).	I hope you're well. I have a very quick query about fibre use with Greenlight. Can I please check if any other fibres, e.g. HP can be used with the Greenlight XPS device or if it is only the moxy fibres. If there are other fibres being used is this under a separate CE marking with yourself? or outside of your company recommendations? I look forward to the call on Friday and will send over the questions tomorrow so you can review prior to the meet. These do not need to be answered before the meeting but we will discuss	Both the MoXY fiber and the HPS 2090 fiber can be used with the console. These are both Boston Scientific manufactured. There are no compatible aftermarket fibers produced by other companies that are compatible with the XPS system. MoXY is the most widely used fiber. HPS 2090 fibers can be used with the older 120W console but when used with the XPS console tend to be used for anatomical enucleation, not vaporization. I hope this answers your question, but if you have any further queries around this please do let us know.

			them in the meeting, along with any questions you may have and any additional data can follow after the call.	Look forward to the discussion on Friday.
2.	26/11/2021	Initial meeting with the Company		Notes from the call: Appendix 2, approved 09/12/2021 Additional information requested on the call: • Company to provide up to date CE certification (Chased 07/12/2021; received 09/12/2021) • Company to provide up to date IFU for the console (Chased 07/12/2021; received 09/12/2021) • Company to provide literature search terms used to identify latest evidence – Provided 02/12/2021 – Appendix 3
3.	28/11/2021	Additional questions sent to clinical experts		Responses received from 8 of 11 experts. Questions and collated responses: Appendix 4
4.	02/11/2021	Additional question sent to clinical experts and the Company	Is “ejaculatory hood sparing GreenLight Laser prostate photoselective vaporization” considered the same as anatomical vaporisation, and in scope?	Responses received from 7 of 11 experts, and also response from the company, collated responses: Appendix 5
5.	25/11/2021	Collated EAQs received from NICE		Appendix 6

6.	20/12/2021	Additional question sent to clinical experts	Is vapo-resection (also referred to as vapo-incision) the same as or comparable to PVP and HoLEP? Is this a commonly used procedure?	Responses received from 8 of 11 experts. Collated responses: Appendix 7
7.	14/01/2022	Additional questions sent to clinical experts		Responses received from 10 of 11 experts. Collated responses: Appendix 8
8.	14/01/2022	Meeting with David Rawlings, Clinical Scientist, Laser Protection Adviser, NuTH, to discuss laser safety requirements for GreenLight c/w HoLEP		Notes from meeting: Appendix 9

Insert more rows as necessary

Appendix 1.

During correspondence with the company and experts, additional information is sometimes included as file attachments, graphics and tables. Any questions that included additional information of this kind is added below in relation to the relevant question/answer:

File attachments/additional information from question X:

Insert

File attachments/additional information from question X:

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File attachments/additional information from question X:

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NICE National Institute for Health and Care Excellence

Appendix 2

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical Technologies Evaluation Programme

Company Engagement Meeting [Zoom]

MT564 Greenlight XPS

Date: **26/11/2021**

Time: **14:00-15:00**

Documents

MTG, 2016: **https://www.nice.org.uk/guidance/mtg29**

MTG update scope 2021: **https://www.nice.org.uk/guidance/indevelopment/gid-mt564/documents**

Attendees:

EAC: Kim Keltie (Newcastle EAC Centre Manager, Project lead), Andrew Sims (Newcastle Centre Director), Joanne Davison (Admin support, notes)

NICE: Samantha Baskerville (lead analyst), Rebecca Brookfield (senior analyst), Ying-Ying Wang (senior analyst), Christopher Pomfrett (Advisor)

Company (Boston Scientific): Alice Craven (HE and Market Access for UK); Glyn Burtt (Medical Director), Emily Woodward (Director HE and Market Access)

AGENDA

Welcome and introductions

EAC discussion around questions from review submission (attached below)

Confidentiality and the Correspondence Log

NB: Further to this meeting, the EAC will communicate directly with the Company (and vice versa), copying NICE in. All correspondence should be via email. ***All correspondence that informs the assessment will be published in the correspondence log on NICE's website as supporting information when the final guidance is published****. It is the Company's responsibility to highlight for redaction any information that is commercially*

sensitive ([redacted]) or academic in confidence ([redacted]).

Next steps:

ACTION: NICE (SB) to forward questions to 11 expert advisors (including 4 nominated by the company) later today (26/11).

ACTION: EAC to maintain log of ongoing correspondence with NICE and present alongside final documentation on product assessment.

CP confirmed leaving NICE on 01/02/2022; RB and YYW will take over.

Timeline:

- EAC report due 19/01/2022.
- Expert committee meeting scheduled 18/022022.
- Adoption resource to be published after with full report.

Questions for further discussion:

1. **Are Greenlight XPS and GreenLEP equivalent?**
    a. Are both conducted at 180 W?

Company [GB] explained no specific requirement to conduct at 180 W but if laser not run at maximum power of 180 W procedure would take longer. Procedure may be conducted anywhere from 5–180 W in 5 W increments, up to the discretion of the operating urologist. More experienced urologists happy to use maximum 180 W; junior doctors possibly more comfortable starting at lower power. 180 W commonly used for vaporisation.

NICE [CP] asked if power was foot-pedal controlled and whether theatre team were required to document all power levels/ranges used in whole procedure. **Company [GB]** explained the power-setting control is located on the console and normally be adjusted by a nurse on surgeon's instruction. Total energy delivered is displayed at end of procedure. Most clinicians are thought to record the power settings and energy delivered in their operating notes.

    b. Are both equivalent (mode of action, training/experience, same consumables)?

Company [GB]: XPS is the name of the console, MoXY is a high energy fibre (single use) used for laser vaporisation of tissue, HPS is a lower energy fibre commonly used for anatomical enucleation (more mechanical process). MoXY fibres require water irrigation through the fibre channel to maintain operating temperature.

> New question: As per the final scope, our EAC will focus on PVP. However, in the literature different terminology is used to describe the use of GreenLight. Terms include: photoselective vaporization of prostate (PVP), anatomic vaporization, vapoenucleation, and en-bloc enucleation. The previous assessment report stated that enucleation was out of scope and that the company considered this off label use – is this still the case?

Company [GB]: Anatomical vaporisation is similar to PVP. Enucleation is not considered off-label, however it is primarily a mechanical process using the endoscope tip. Holium lasers (HoLEP) as a comparator conduct more enucleation, and minimum amount of vaporisation. Greenlight XPS mainly used for vaporisation.

NICE [CP]: Confirmed that scope is in line with CG197 terminology. Company can notify different use case (enucleation) to NICE, but would be treated as different NICE output.

2. **Can HPS and MoXY both be used for GreenLight XPS? Are there are other fibres being used?**

Company correspondence (via email): Both the MoXY fibre and the HPS 2090 fibre can be used with the console. These are both Boston Scientific manufactured. There are no compatible aftermarket fibres produced by other companies that are compatible with the XPS system. MoXY is the most widely used fibre. HPS 2090 fibres can be used with the older 120 W console but when used with the XPS console tend to be used for anatomical enucleation, not vaporisation.

Company [GB]: HPS is not as efficient, narrower beam diameter, and cannot run at 180 W due to fibre degradation caused by heating.
NICE [SB] asked if replacement fibres to be supplied by Boston free of charge; **Company [GB]** confirmed replaced under normal warranty conditions. One fibre use per patient guarantee (even if second fibre necessary due to prostate size, this is provided free of charge). Capital cost of console not included in original model, commercial agreement with trusts in the number of fibres purchased.

3. **Can HPS and MoXY fibres both be used for GreenLEP?**
   From above, GreenLEP is out of scope

4. **The EAC notes that different power settings are reported in the literature (80 W, 120 W, 180 W).**
   a. Do the different power setting have different instructions or indication for use?
      Company [GB] explained higher power settings resulted in faster vaporisation. No difference in indication for use. Only difference in instructions for use is the use of a cool bag with 180 W console to reduce fibre degradation.

   b. Are we correct in understanding the 180 W can be used on a lower setting? If so, what is the range of power that the XPS can provide and how do you understand this is used in practice? Is a lower power used at start and increased?

   Company [GB]: Vaporisation conducted over a range of power (5 W to 180 W). The energy delivered depends on several factors in addition to the power setting, including laser beam divergence and operating distance. Typically start using lower power to clear the area. Theatre team may not record power setting used. Console output shows total energy delivered across the procedure, this may be recorded in operating notes.

5. **Can the company send through the latest CE certification?**
   ACTION: Company to provide up to date CE certification (submit to NICE Docs w/c 29/11)

6. **Can the company send through latest IFU please?**
   ACTION: Company to provide up to date IFU (submit to NICE Docs w/c 29/11)

7. **Can the company send a copy of the search used for the evidence review submission for EAC critique?**

   ACTION: Company to provide literature search terms used to identify latest evidence (submit to NICE Docs w/c 29/11)

   ACTION: Company to keep NICE informed of paper submitted academic in confidence.

8. **Supply of Consumables**

NICE [SB] queried the supply of safety goggles.
Company [GB] confirmed that goggles for green light at 532 nm) can be purchased from a range of suppliers. Company also confirmed that blinds, and shutters do not require changing (same as Holmium laser), however door signs would need updating.

9. **Laser Safety**

EAC [AJS] queried if an expert Laser Protection Adviser was included in previous assessment/MTAC to advise on implementation costs for end-users.

ACTION: EAC to identify local source or independent person to advise on laser safety.

10. **Diversity and Inclusion**

NICE [CP] questioned whether evidence was available in Transgender population. Company [GB] stated that scarring of the urethra is the challenge for any surgical prostate intervention (not specific to GreenLight). Long-term oestrogen reduces the size of the prostate, such that surgical prostate intervention would be rare.

ACTION: Company to share anecdotal evidence (if available).

11. **Adoption and implementation**

NICE [CP] explained that NICE are removing patient pathways from website. NICE interested in enhanced adoption support resource and guidance tools to promote product to end-users (i.e. when to use GreenLight over other prostate interventions). This will be displayed in a matrix to make clearer to commissioners.

Appendix 3

Search Strategy

Purpose: in support of a NICE submission on the use of BSC's (formerly AMS/American Medical Systems) GreenLight (XPS, Moxy, 180-W) system for photoselective vaporization of the prostate (PVP) to treat benign prostatic hyperplasia (BPH).

Bibliography includes: 75 references.

Four databases are searched using the below criteria and strategy. The databases are:

- MEDLINE (references added to database January 2020 to present [date search is run]) is produced by the National Library of Medicine (US) and includes more than 15 million references to the world's biomedical journal literature.

- Embase (references added to database January 2020 to present [date search is run]) is an Elsevier product and includes over 7,000 international biomedical journals. Meeting abstracts from major medical conferences began to be added in late 2010.

- Cochrane Library, includes the Cochrane Database of Systematic Reviews (CDSR) (publication years 2020-2021) is a journal and database for systematic reviews in health care. CDSR includes Cochrane Reviews (systematic reviews) and protocols for Cochrane Reviews as well as editorials and supplements. Available at: https://www.cochranelibrary.com/

- HTA Database (publication years 2020-2021) provides access to bibliographic information about ongoing and published health technology assessments commissioned or undertaken by HTA organisations from around the world. Available at: https://database.inahta.org/

The literature search strategy/scope of work is determined by the review of the literature. This process is facilitated by the Principal Librarian. Once the Principal Librarian obtains the scope of the search and criteria from the reviewer, the search is completed in a series of steps. Each step is designed to bring the search results from broad to narrow, by using advanced Boolean search logic for information retrieval within databases*.

*For basic information on Boolean logic see this National Library of Medicine (US) tutorial: http://www.nlm.nih.gov/bsd/disted/pubmedtutorial/020_360.html

Search Criteria

Search criteria is defined as what is included in the search (and therefore illustrated what is also not included).

Literature Search Inclusion Criteria

- Topic: Use of BSC's (formerly AMS/American Medical Systems) GreenLight (XPS, Moxy or 180-W) system for photoselective vaporization of the prostate (PVP) to treat benign prostatic hyperplasia (BPH).

- Document types: clinical studies (including meta-analyses and systematic reviews)
- Language: English language full-text
- Databases: Embase (via Embase.com); Medline (via OVID); Cochrane Library & HTA (via their websites)
- Time period: January 2020 to present

Search Strategy

The search strategy below is determined by the Search Criteria (mentioned above) and employed within research databases using Boolean logic for information retrieval. Each search "set" progresses the overall search results from general to specific findings. The search strategy is captured below to illustrate the precise search approach taken to yield search results.

Database used: Embase (includes MEDLINE subset) via Embase.com

Accessed: July 29, 2021

Downloaded results: Set #11 (98 references)

No.	Query	Results
#11	#10 NOT 'conference abstract'/it	98
#10	#4 AND #8 AND [english]/lim AND [1-1-2020]/sd	131
#9	#4 AND #8	1329
#8	#5 OR #6 OR #7	49226
#7	'prostate hypertrophy'/exp	40776
#6	prostat* NEAR/5 (hypertroph* OR hyperplas* OR enlarg* OR bph OR bpe OR obstruct*)	49208
#5	(bph OR bpe) NEAR/5 (prostat* OR hypertroph* OR hyperplas*)	14552
#4	#1 OR #2 OR #3	5424
#3	'greenlight laser'/exp OR 'greenlight'/exp OR 'photoselective vaporization of the prostate'/exp OR 'photoselective vaporization'/exp	143
#2	(532nm OR '532 nm' OR ktp OR xps OR hps OR pv OR pvp OR photoselect* OR 'photo selective' OR lbo OR 120w OR '120 w' OR 180w OR '180 w' OR moxy OR 'high performance system') NEAR/10 (laser OR vaporisation OR vaporization OR photovapori* OR bsc OR bsci OR boston OR ams OR 'american medical' OR 'american med')	4793
#1	(greenlight OR 'green light*' OR greenlighttm) AND (laser OR lasers OR 532nm OR '532 nm' OR ktp OR xps OR hps OR pv OR pvp OR photoselect* OR 'photo selective' OR lbo OR 120w OR '120 w' OR 180w OR '180 w' OR moxy OR 'high performance system' OR vaporization OR vaporisation)	1513

Database used: MEDLINE (full database) via OVID

Accessed: July 29, 2021

Downloaded results: Set #13 (68 references)

#	Searches	Results
1	((greenlight or "green light" or "green lighttm" or greenlighttm) adj10 (ams or bsc or bsci or boston or "american med" or "american medical")).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	27
2	(greenlight or greenlighttm or "green light" or "green lighttm").mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	3706
3	(laser or lasers or 532nm or "532 nm" or ktp or xps or hps or pv or PVP or photoselect* or "photo selective" or LBO or 120w or "120 w" or 180w or "180 w" or moxy or "high performance system" or vaporization or vaporisation or photovapor*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	391699
4	2 and 3	866
5	((532nm or "532 nm" or ktp or xps or hps or pv or pvp or photoselect* or "photo selective" or lbo or 120w or "120 w" or 180w or "180 w" or moxy or "high performance system") adj10 (laser or vaporisation or vaporization or photovapor* or bsc or bsci or boston or ams or "american medical" or "american med")).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	3774
6	1 or 4 or 5	4218
7	((Bph or bpe) adj5 (prostat* or hypertroph* or hyperplas*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	9707
8	(Prostat* adj5 (hypertroph* or hyperplas* or enlarg* or bph or bpe or obstruct*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	31795

9	Prostatic Hyperplasia/	22560
10	7 or 8 or 9	31809
11	6 and 10	737
12	limit 11 to dt=20200101-20210729	75
13	limit 12 to english language	68

Search Engine: Cochrane Library

Accessed: July 29, 2021

Downloaded results: 3 references

Search Terms: greenlight or “green light” or green-light

Publication Years: 2020-2021

Search Engine: HTA Database

Accessed: July 29, 2021

Downloaded results: 1 reference

Search Terms: greenlight or “green light” or green-light

Publication Years: 2020-2021

Librarian’s Reference Selection Criteria

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Appendix 4

Greenlight clinical expert engagement questions

Greenlight XPS documents can be found below:
MTG **https://www.nice.org.uk/guidance/mtg29** and updated scope: **https://www.nice.org.uk/guidance/indevelopment/gid-mt564/documents**

NICE Guidance on Greenlight XPS, in 2016, supported its use in the general population. However previously there was not sufficient evidence base to support its use in the high-risk population. We know that experts value the technology in this high-risk population and are keen to understand some of the below aspects in practice so any comments you can provide would be much appreciated.

Expert contact details and declarations of interest:

Expert #1	Gordon Muir, Consultant Urologist, King's College and London Bridge Hospitals [redacted]
	Nominated by: NICE and company
	DOI: 2009 - present : Mentor and consultant BSCI; 2018 – present: Mentor and consultant Olympus GMBH; 2013-2019 – present: Mentor and consultant Neotract
Expert #2	Richard Hindley, Consultant Urologist, Clinical Lead for Urology and Visiting Professor, Hampshire Hospitals NHS FT, [redacted]
	Nominated by: n/a
	DOI: From approx. 2010: I do receive ad hoc payments as a clinical advisor and proctor for Boston Scientific; I was involved with the GOLIATH trial
Expert #3	Mr Amr Emara, Consultant Urologist, Hampshire Hospitals Foundation Trust, [redacted]
	Nominated by: company
	DOI: none
Expert #4	Marios Hadjipavlou, Consultant Urological Surgeon, Guy's & St Thomas' NHS Foundation Trust [redacted]
	Nominated by: NICE
	DOI: none

Expert #5	Maya Harris, Consultant Urological Surgeon, South Warwickshire NHS Foundation Trust, [redacted]
	Nominated by: NICE
	DOI: none
Expert #6	Sanjay Rajpal, Consultant Urologist, Sheffield Teaching Hospitals [redacted]
	Nominated by: company
	DOI: 29/09/21 I have received payment for proctoring services from Boston Scientific (manufacturer of the GreenLight XPS)
Expert #7	Ian Pearce, Consultant Urological surgeon, Manchester University NHS Foundation [redacted]
	Nominated by: NICE
	DOI: none
Expert #8	Aniruddha Chakravarti, Consultant Urological Surgeon, The Royal Wolverhampton Hospitals NHS Trust, [redacted]
	Nominated by: NICE
	DOI: Provided expert opinion on Urolift procedure

SETTING:

1. NICE recommends that hospitals adopting Greenlight XPS plan for service redesign to ensure that day-case treatment can be delivered appropriately. Is this appropriate for both non high risk and high risk populations? Are there specific indications or scenarios where you would not proceed with day case care? Could you estimate day-case procedure rates in your Trust?

Expert #1	Yes for high risk. We have 90%+ day care. Can be 100% with 23 hour stay or hospital hotel. Only very high risk or social cases need overnight bed if morning lists utilised
Expert #2	Day-case rates have varied at between 40-60% -we can do better than this but our day unit has beds for an overnight stay which has hindered my desire to achieve 70%+ which I believe is not difficult to achieve.
Expert #3	Although Greenlight PVP is safer with higher risk group but this particular group require careful assessment in general – however is it a multifactorial decision; for example if mildly enlarged prostate with straight forward, short procedure and mild co-morbidities such as AF, then day-case procedure is still amenable – therefore the

	final decision for day case procedures should be patient tailored. In general majority of patients could be day case procedure (less than 24 hours hospital-stay) – My estimated average of 80% achieving this target.
Expert #4	Yes – the technology itself is safe for high and non-high risk populations, as long as they are fit for general or spinal anaesthesia. High risk patients may require overnight stay for medical/anaesthetic reasons rather than surgical reasons. A very rough estimated day case rate would be 80%, as prostate enlargement is mainly a condition of the ageing population.
Expert #5	I think about 90% of Greenlight XPS cases could be done as a day case. Occasionally, the patient with a prostate > 100 cc would need to stay due to the bladder irrigation
Expert #6	Yes -day case treatment using Greenlight XPS is feasible in both non-high risk and high risk patients. The scenarios where day case would not be considered are • Patient factors: High anaesthetic risks (needs postop monitoring), frailty, social reasons (lives on his own) • Procedure factors: Conversion to TURP, combined with additional procedure like bladder stone treatment or bladder tumour removal Our day case rates are around 80%
Expert #7	Day case procedures are suitable for both high and non-high risk patients. The only reason not to progress with day case surgery would be in those patients not fulfilling the BADS criteria e.g. : Living alone, and perhaps those patients living a significant distance away or who may require extra input e.g. : haematology for documented bleeding disorders
Expert #8	Day case procedure where patients are discharged on the same day of the procedure without a catheter are only possible for small prostates and relatively fit patients who are not in chronic retention and do not have many co morbidities. In my opinion this would be possible in about 25% patients in the cohort that undergoes BPH surgery in my Trust.

2. Please could you describe the additional theatre requirements for the Greenlight laser setting and the practicality of these being implemented?

Expert #1	Standard laser protection
Expert #2	A laser safe theatre plus laser safety certification for the surgeon. No major issues here.
Expert #3	Theatre requirement: Laser safe theatre with the compatible plug in electrical supply + the Green-light safe googles and trained laser officer.

Expert #4	The theatre needs to be laser-safe. This includes installation of window blinds, high power socket, signage, laser goggles, as well as training and a laser safety officer. Most hospitals have some theatre rooms that have already been modified for other laser procedures.
Expert #5	Laser machine (with fibres and glasses), laser-safe theatre, staff training
Expert #6	In addition to the laser machine, fibres and safety googles, the operating theatres need to laser safe as per the local trust laser safety officer's guidance. A special wall socket for powering the laser will be needed (not too cumbersome or restrictive as most urology units use holmium laser for stone disease and may already have some or most of these provisions already made in theatres) The kit used for TURP can be safely used with the addition of a laser bridge (purchased separately) along with changing the tip of resectoscope sheath to metal from ceramic (can be easily done by the manufacturer of the kit like Karl Storz, Olympus). The operating time for the procedure is approximately 15% longer than a TURP (again this would depend on the prostate volume), so this needs factoring when planning lists.
Expert #7	The only additional requirement would be for the equipment itself
Expert #8	The Greenlight laser has a very bright green beam of 532nm wavelength and has properties of higher divergence and hazard distance thereby making it risky for human eyes. Hence laser protection measures such as high level eye protection for ALL theatre personnel and patient is essential and theatre door protection is needed as per laser safety guidelines. All users must be certified as having completed the necessary laser safety training that needs updating at specified times. There is also need for a special camera filter and the laser can be delivered by cooled special fibres called 'MoXy' fibres.

TECHNOLOGY:

3. This guidance update will focus on 180W (in line with original guidance). However some evidence suggests that procedures start with lower power (80W) and increased to 180W. Is it now standard practice using GreenLight XPS? Have you seen differences in previous lower powered devices in procedure or outcomes? We understand the 180W can be used at different settings, can you explain for what scenarios or individuals you adjust this?

Expert #1	Up to experience of user and prostate volume. I tend to use 180w all the time, trainees start on 120w and work up
Expert #2	In a patient with a smaller gland or an increased risk of bleeding I will tend to vaporise at lower energy settings – say 120-130W but for a large gland I may go up to 170-180W. I do not routinely vaporise at 180W as there is a

	small increased risk of bleeding and capsular perforation and this needs to be balanced with the risks and slightly longer time to perform the procedure at lower energy settings. 180W in my opinion is not required for smaller glands. I rarely require a 3-way catheter.
Expert #3	The standard practice now is the XPS 180W GL using the Moxy fibre, different surgeons will adapt different techniques. In general most surgeons will start with lower energy and reach the 160-180W soon after for quicker and more effective vaporisation. Lower powered devices consumed longer time with less effective size reduction. Different setting depend on prostate size – there is general concept that lower energy to start with can achieve better coagulative effect and decrease risk of early bleeding (that can affect vision), however many surgeons will start at higher energy with no noticeable difference.
Expert #4	Without having any personal experience, I am aware from colleagues that the newer 180W XPS Greenlight is much more powerful, therefore quicker, more effective and with better haemostasis. Therefore any data on the older 80W Greenlight are probably not relevant, in my opinion. I am not familiar with the settings of the 180W device.
Expert #5	The procedure is usually started with a low power (80W) to delineate the anatomical limits of vaporisation. Subsequent use of higher power (up to 180W) allows quick and safe vaporisaton of the tissue. I do not have experience of the previous generations of Green Light laser machines.
Expert #6	It is standard practice to start at lower power settings and increase the power. At the start of the procedure, there is little space to for the laser fibre to be manipulated (due to the occlusive prostate) and using high power at this stage risks damaging the fibre (resulting in reduced efficiency of the fibre). Hence, we start at low power settings and once there is some space in the prostatic urethra, we move to higher power settings for effective vaporisation and volume clearance.
Expert #7	I do not know if it is now standard practice. Settings are often changed according to intra-operative findings and experience but no definite rules exist and this is based largely on operator preference
Expert #8	I had used the HPS system in around 2007 which was 80W and then up-graded to 120W. I have later used the XPS system with 180W and it is a huge improvement enabling the surgeon to treat larger prostates more effectively. The power can be reduced to 80W as and when necessary particularly when using the laser near the apex or on the bladder neck. The coagulation mode at a lower setting is also useful to control bleeding.

4. Is the procedure “photoselective vaporisation of the prostate (PVP)” exclusive to GreenLight? Can any other devices (other than GreenLight) be used to conduct PVP? If yes, do any other devices use 180W?

Expert #1	No

Expert #2	Not that I am aware of.
Expert #3	Yes PVP is exclusive to greenlight – originally based on the (532-nm) photoselective wave-length achieved by passing Nd:Yag laser through KTP crystal to half the wave-length in the older 60 & 80W models, and then in 2012/13 this was modified to the LBO (Lithium Triborate) in the XPS 180W generator.
Expert #4	I am not aware of any other devices in the UK that are used for PVP. Generally, PVP is synonymous to Greenlight and the terms are used interchangeably.
Expert #5	In addition to GreenLight, Thulium laser vapo-enucleation is described in the literature, but I do not have experience of it myself.
Expert #6	Yes PVP is exclusive to Greenlight. Other devices like Thullium and Holium laser can also be used for vaporisation of the prostate. They use different power (not 180W)
Expert #7	Greenlight laser provides photoselective vaporisation but vaporisation can also be achieved with diathermy (heat) and over a longer time period, Rezum (steam treatment and vaporisation)
Expert #8	Vaporisation of prostate can be achieved using a bipolar electrode (Vapo-trode or button electrode) quite effectively with same outcome. It also can be done with other lasers like thulium laser. So vaporisation as a technique to ablate the adenomatous part of the enlarged prostate in order to produce a cavity in the prostatic urethra thereby treating bladder outflow obstruction from an enlarged prostate can be achieved by several means including water jet (aquablation).

TECHNIQUE:

5. In the literature different terminology is used to describe the use of GreenLight. Starting from standard vaporization to anatomic vaporization, then to vapoenucleation, and finally to en bloc enucleation. Is all the above terminology describing different surgical techniques using GreenLight XPS? Are all equivalent? (requires the same equipment, training etc)? Can all be conducted using 180W? Are all surgical techniques within Final Scope? These different procedures appear to have their own comparator, e.g. HoLEP, PEBE, TURIS, mTURP/bTURP, are all comparators within scope if all Greenlight procedures are? Is there a guide for what is the best comparator for each?

Expert #1	The laser can be used for all techniques. GreenLEP may not be suitable for day care, like HoLEP
Expert #2	Yes all of these techniques can be used with the GL PVP 180W laser – however the laser fibre can be changed to an older type of fibre (HPS) which tends to be used for GreenLEP. I do not offer GreenLEP currently. A morcellator would be required for this technique (as per HoLEP). This has a cost of approx. £30,000. I do standard vaporisation and anatomical which essentially means lasering tissue away until reaching the capsule of

	the prostate as per TURP. I sometimes will vapoenucleate a median lobe if very large and then instead of using a morcellator which we don't have I will switch to the resectoscope to make a big lump of tissue into smaller pieces to allow safe removal. I don't do this very option. I would categorise standard PVP and anatomical together.
Expert #3	I agree all above terminology describe different techniques – the original technique is the standard vaporisation, the anatomic vaporisation is a modification of the same, reflecting mainly surgeon experience and his place in the learning curve. Theoretically, it can achieve more volume reduction and does not require additional equipment. Vapoenucleation or GreenLep is mirroring the HoLep technique and require extra equipment mainly morcellator and relative accessories. As expected enucleation techniques achieve more size reduction however this will carry higher risk of side effects (Ejaculatory dysfunction/stress incontinence/bladder injury/transfusion requirement) - They can all be conducted by the 180W generator however enucleation may use the older 120W fibre rather than the MoXy fibre.
Expert #4	These techniques are all very different, yet some are overlapping. Enucleating techniques (such as Greenlight enucleation, or HoLEP) remove much more tissue, therefore produce longer lasting results – i.e., the reintervention rate is generally lower than non-enucleating techniques, such as standard PVP or TURP. Enucleating techniques are more beneficial for patients with very large prostates (i.e. over 70 or 80mL). The equipment required for the various Greenlight techniques is the same, but training generally takes much longer for enucleating techniques as it is technically more challenging, and potentially with a slightly higher risk of postoperative incontinence in certain cases. I believe all techniques can be conducted with a 180W device. I think there is no right or wrong comparator – it simply depends whether one is assessing the method (i.e. enucleating techniques Vs vaporising Vs resecting) or the technology (i.e. Greenlight Laser Vs Holmium Laser Vs TURP). I think most urologist would agree that of all enucleating techniques (i.e. holmium laser, greenlight laser, bipolar enucleation), HoLEP is probably the easier to learn and master.
Expert #5	I do not think that vapoenucleation, and finally to en bloc enucleation should be part of the review, as they are not used widely and are similar to HoLEP done with GreenLight laser. mTURP/bTURP are the most appropriate comparators and TURIS is synonymous to bTURP. I am not sure what PEBE is.
Expert #6	Standard vaporization,anatomic vaporization, vapoenucleation, and en bloc enucleation are different surgical techniques using Greenlight XPS. They are all not equivalent. All of them can be conducted using the 180W laser machine Enucleation procedures require additional training (has a longer learning curve) and will need different laser fibre (120W, GLL fibre) and also a morcellator. Standard vaporisation should be only used in the final scope Comparator for this would be mTURP/bTURP/TURIS
Expert #7	*Is all the above terminology describing different surgical techniques using GreenLight XPS?* These are essentially different terms for achieving the same outcome *Are all equivalent? (requires the same equipment, training etc)?*

	Pretty much, yes *Can all be conducted using 180W? Are all surgical techniques within Final Scope?* Yes and yes *These different procedures appear to have their own comparator, e.g. HoLEP, PEBE, TURIS, mTURP/bTURP, are all comparators within scope if all Greenlight procedures are? Is there a guide for what is the best comparator for each?* I would say that the comparators should all be the same since the desired outcome is on of quality of life. HoLEP and TURP are the maintwo comparators for all these procedures
Expert #8	Use of various forms of technology and sometimes the same technology in different techniques to treat bladder outflow obstruction from an enlarged prostate can make comparators confusing and often there is paucity of evidence in terms of RCTs with head to head comparison. Evidence from real world data remains the only source for comparison but are often unreliable. In summary bladder outflow obstruction caused by benign enlargement of prostate can be treated by: A) Cavity producing means a) creating a cavity in prostatic urethra by removing enlarged prostate tissue (adenoma) - this can be achieved by: 1) transurethral resection (coring out from inside) of adenoma by monopolar cautery (mTURP) or bipolar cautery (bTURP or TURis) or combined vapo-resection using Thulium, Holmium or Greenlight laser. 2) transurethral enucleation (enucleation of adenoma in ana-tomical plane) of adenoma by using electrocautery (usually bipolar) or laser energy eg. Holmium laser enucleation (HoLEP), Thulium laser enucleation (ThuLEP) or Greenlight laser enucleation (GreenLEP), photoselective en bloc enucleation (PEBE). 3) Transurethral ablation of adenoma to create an immediate cavity using laser energy by Greenlight photovaporisation (PVP), which can be standard PVP to produce a cavity enough to open the bladder outflow or anatomical PVP to ablate entire thickness of adenoma to the anatomical plane, Thulium laser vaporisation, bipolar electrocautery vaporisation (TUVP using vapotrode) or Aquablation using water jet (under development). This method does not enable any removal of tissue for analysis and regrowth of adenoma can happen causing a reintervention in less than ten years. The durability of an achieved desired outcome is less compared to enucleation techniques in anatomical plane. b) non cavity producing (no tissue resected or ablated to produce an immediate cavity) but a channel is intended to open an obstructed bladder outflow - 1) medical therapy

	2) Urolift 3) REZUM The desired outcome of all procedures is relief of symptoms from opening up of an obstructed bladder outflow but the outcome measures (IPSS, urine flow rate) are not comparable between the different treatment groups. Similarly, the durability of desired outcome is also significantly different across the treatment groups. The comparator techniques should be those used within a particular group (as above).

6. Some of the evidence refers to GreenLEP. Is this enucleation? Can GreenLight and GreenLEP be considered equivalent (i.e. is guidance on GreenLight applicable to GreenLEP?).

Expert #1	Enucleation is a technique which removes more tissue, needs higher surgical skill levels, and may have higher complication rates and a need for overnight stay. It matters not which energy source is used.
Expert #2	This could all be covered in the same guidance – perhaps to state that in certain circumstances these techniques can be used – however, you may wish not to include in the guidance – this is an area for discussion.
Expert #3	GreenLeP /enucleation en bloc, all refer to enucleation technique rather than vaporisation technique and the comparator should be the HoLep not TURP or PVP – I would be shy to put GreenLep in same basket with PVP.
Expert #4	Yes – GreenLEP is enucleation using Greenlight. As discussed above, Greenlight PVP and GreenLEP are separate procedures and I don't believe they should be considered equivalent.
Expert #5	As above, GreenLEP is an enucleation technique and should be excluded from the review, as it is not used widely.
Expert #6	This is enucleation -Not equivalent and current guidance is not applicable to it
Expert #7	*Some of the evidence refers to GreenLEP. Is this enucleation?* Yes *Can GreenLight and GreenLEP be considered equivalent (i.e. is guidance on GreenLight applicable to GreenLEP?).* Yes
Expert #8	Explained above [Question 5]. Ideally separate guidance required for Greenlight vaporisation (PVP) and Greenlight enucleation (GreenLEP).

IMPLEMENTATION

7. Are there any barriers to implementation of the procedure in this setting, e.g. anaesthesia staffing and capacity. What are the training needs and is there a learning curve with the technology?

Expert #1	Yes. Good simulator which we have validated. Learning curve to competence about 25 cases.
Expert #2	Yes there is a learning curve – perhaps 20 cases to get up and running independently and in the order of 100 cases to be able to take on larger glands over 80mls. I have performed or supervised over 1500.
Expert #3	Greenlight PVP is a straight forward procedure to adapt, however as any other surgical or endoscopic procedure there will be a learning curve – definitely far less compared to TURP and trivial when compared to HoLep – all endoscopic and new techniques learning curve depend largely on the experience of the surgeon in this field (well established consultant will be expected to achieve shorter learning curve compared to a new consultant/ trainee) – I would quote average between 25-50 cases to achieve high standards of vaporisation
Expert #4	There are no specific barriers to implementation, apart from the need for laser training of clinical and nursing staff, and laser safety precautions in theatre. This is considered an easy procedure to learn and master – estimated 20-30 cases.
Expert #5	I do not think there are anaestheic concerns regarding the procedure. The surgeon will require a mentorship over 10-20 procedures and the staff will require laser-safety training and a non-scrub additional laser operator in the theatre (usually a senior theatre nurse).
Expert #6	Barriers would include: • Capital costs of the laser machine and fibre costs • Can be safely carried out in day case settings (many centres have moved this treatment to their Spoke hospitals and successfully implemented the service). So support needed for any day case procedure (in terms theatre staff and anaesthetic cover) • Training includes- spending time (minimum of 8-10 hours) on high fidelity simulator (supported by the manufacturer) followed by clinical proctorship in operating theatres (supported by the manufacturer). The learning curve is around 15-20 procedures. • Perception among urologists that this laser results in sub-optimal tissue clearance (higher risk of secondary interventions), post op prolonged dysuria, prostatitis- all of these are related to the 80W GLL, but rarely seen in the 180W XPS system.
Expert #7	The challenge is really the cost of the equipment and the challenge from newer less invasive techniques e.g. : Rezum. And those with a more impressive track record e.g. : HoLEP There is a learning curve also and staff training will be required for laser use
Expert #8	All theatre staff needs to be trained in laser safety protocol. There should be a lead person in theatre who will be the laser safety operator who will under-go more extensive training. Theatre doors and signs should be up to the safety standards. An anaesthetist will be required as this procedure cannot be done under local anaesthesia. Irrigating fluids and someone to run and monitor those fluids would be required in theatre.

	The surgical learning curve is steeper for enucleation and relatively straight-forward for vaporisation/ablation. Simulations available for training.

8. If the wattage of the device was increased in future, would the guidance remain relevant?

Expert #1	Any change in the delivery system relating to increased power should be assessed for safety but probably no need for large RCT's if cohort studies show equivalence or superiority
Expert #2	I don't think it will be. If it was the yes it would remain relevant.
Expert #3	I think increased wattage will be an advantage, however relative evidence should be considered when this technology emerge
Expert #4	I am not sure.
Expert #5	I do not expect the procedure will change much in the future, as 180W laser has excellent performance.
Expert #6	Yes
Expert #7	Probably yes
Expert #8	Most likely unless the surgical technique changes significantly.

9. Any experience in using Moxy/HPS fibres and comments on reliability; e.g. is it one per patient unless used for larger prostate? Any comments on wastage of consumables associated with the procedure?

Expert #1	Very large prostates or poor technique may mean 2 fibres needed – currently the company does not charge for a second fibre
Expert #2	In less than 1% is a second fiber necessary. A second fiber will be required for a massive gland but in the remit of this guidance is probably not relevant as PVP should probably be for gland volumes <120mls.
Expert #3	I currently use Moxy fibers only, and I don't recall using more than one fiber in single case except in three occasions over the past 8 years of using it, mostly faulty fibers but once for huge prostate (running out of energy limit/fiber)
Expert #4	I do not know the answer to these questions unfortunately as I don't use this technology.
Expert #5	The fibres are usually quite reliable. Fibre wastage depends on the surgeon's technique and experience, as fibres get broken with difficulty in access.

Expert #6	Yes one fibre would suffice for most patients (assuming treating prostates up to 100g) Laser fibre can be disposed in the yellow clinical waste bin. When compared to TURP, there are less comsumables – during this procedure we use saline at room temperature (in comparasion for TURP- warm saline or glycine is used), post op irrigation is none or limited to 1 bag. The heating of irrigation fluid, disposing the empty bags are eliminated by this procedure, potentially having a positive influence on reducing wastage.
Expert #7	Sorry, no experience
Expert #8	Yes I have used MoXy fibres with the XPS system and it is a mandatory requirement for the XPS system. Number required is dependent on surgical training and use, but for small - medium size prostates usually one fibre should be enough. Large prostates may require multiple fibres. There will be wasted consumables and guidance will be required regarding environment friendly disposal methods.

POPULATION:

10. Are there specific indications that you would suggest Greenlight for as part of your decision making with patients? Considering in particular if your practice with Greenlight includes high risk groups of individuals with larger prostate sizes, urinary retention and risk of bleeding and if not why not?

Expert #1	We give patients options including their desire for sexual function, prostate size and volume, and personal risk factors
Expert #2	It is my favoured technique if there is an increased risk of bleeding. It is also very safe for patients with an indwelling catheter. I always use GreenLight rather than TURP in appropriate patients.
Expert #3	Limitations are mainly size related – especially when we are describing huge of mega-prostates (180-200+ cc), however in higher risk cases I feel confident to use Greenlight PVP.
Expert #4	Greenlight PVP is an option that should be offered to most patients requiring bladder outflow surgery with a prostate <80-100cc. Because of it's haemostatic option, it might be a preferable option over other procedures, such as TURP or Rezum, in patients with high risk of bleeding (e.g. on anticoagulants).
Expert #5	My practice of GreenLight laser prostatectomy includes patients with larger prostates, in retention and also on anticoagulation. I usually discuss the procedure alongside the other options I offer, such as TURP, Rezum and Urolift and mention PAE, available in the neighbouring trust. Depending on the patients' values and clinical

	situation, they decide whether to go ahead with one or the other procedure as a part of shared decision making process.
Expert #6	We started using GLL in mid-2018 (got GLL after recommendations from the GIRFT review). After our first 100 cases- we have been offering this as the default procedure in our unit in place of TURP. We offer it for urinary retention, patients on anticoagulants / anti-platelet agents and would limit it to a prostate volume of 100cc for all indications. With increasing experience we are offering the procedure to selected patients with prostate volume >100cc The only group of patients we have stopped offering GLL are those who have undergone radiotherapy for prostate cancer. In this groups of patients due to tissue ischaemia (as a consequence of radiotherapy) post-operative outcomes have been unsatisfactory, at least in our cohort (3 patients).
Expert #7	Larger prostates definitely, and also those patients at high risk during anaesthesia
Expert #8	My preference is to do Holmium laser enucleation (HoLEP) for high risk cases such as large prostates with retention of urine, particularly chronic retention as this procedure has the highest success rate and the lowest reintervention rate in twenty years compared to all other procedures. Greenlight laser vaporisation (PVP) may be considered in the elderly with co morbidities with a small-medium size prostate where a quicker ablative procedure will give them symptom relief up to 5-10 years. A less invasive and quicker procedure definitely has benefit in this group of patients. It can also be considered for larger prostates keeping in mind the higher reintervention rates compared to HoLEP.

11. Three high-risk groups are defined in the final scope, would ASAPS classification III and IV be considered high-risk?

Expert #1	Yes – many anaesthetists would be unhappy offering TURP anaesthesia, or day care anaesthesia for these patients
Expert #2	Yes
Expert #3	I assume you mean ASA classification – I agree with the three high-risk groups in the “final scope” as high risk patients and possibly add to this the ASA IV but not III
Expert #4	Yes
Expert #5	The patients with ASAIII are suitable for the procedure, however, patients with ASA IV are not usually offered it as it requires general anaesthetic and any elective surgery is considered to be too high risk in this group.
Expert #6	Generally speaking, ASAPS III and IV are considered high- risk for any procedure necessitating an anaesthetic. Cannot see any reason for adding them to the final scope for this procedure.
Expert #7	From an anaesthetic perspective yes but most procedures would be able to be performed on ASA 3 patients

Expert #8	Yes, high ASA scores and bleeding disorders or anticoagulant use, implanted defibrillator, all should be considered as high risk.

12. What are indications for use for 5 alpha reductase inhibitors? Are those receiving this treatment considered high risk?

Expert #1	Medical treatment of larger prostates. Use of 5ARI actually makes all prostate surgery a little safer by reducing bleeding in all studies so far reported
Expert #2	No – it makes the surgery easier I think.
Expert #3	No foreseen risk with 5 alpha reductase inhibitors but can sometimes be an advantage, possibly decreasing the risk of bleeding.
Expert #4	There are specific NICE recommendations for use of 5aRI. From CG97: 1.4.5 Offer a 5 alpha reductase inhibitor to men with LUTS who have prostates estimated to be larger than 30 g or a PSA level greater than 1.4 ng/ml, and who are considered to be at high risk of progression (for example, older men). [2010] 1.4.6 Consider offering a combination of an alpha blocker and a 5 alpha reductase inhibitor to men with bothersome moderate to severe LUTS and prostates estimated to be larger than 30 g or a PSA level greater than 1.4 ng/ml. [2010] They are not necessarily used for high risk patients, but they are often used for symptomatic patients that are not fit, or want to avoid surgery. Another indication for 5aRI apart from LUTS is refractory haematuria from BPH – they can be useful in this scenario, again if patient not fit for surgery.
Expert #5	I have not had any difficulty with the patients on 5 alpha reductase inhibitors with the current laser. I think it used to be a problem with the less powerful machines.
Expert #6	This medication is used to optimise urinary tract symptoms in men with prostate greater than 30g. Those receiving this treatment would not be considered high risk.
Expert #7	These medications essentially block testosterone from stimulating the prostate and cause a degree of shrinkage but patients taking them are not necessarily high risk
Expert #8	5 alpha reductase inhibitors are used to reduce the size of prostatic adenoma by interfering with testosterone mediated growth of adenoma. They can reduce prostate size up to 25%. No, I cannot see any reason why patients taking this medication should be high risk.

13. Would different power settings would be used for different high risk groups?

Expert #1	No

Expert #2	Lower power settings for those at increased risk of bleeding can be helpful.
Expert #3	In my opinion no relation between high risk groups and power settings.– it is more related to prostate size and operator preference.
Expert #4	I do not know.
Expert #5	No
Expert #6	No
Expert #7	No
Expert #8	Power settings depend on how much volume ablation is required over what period of time and depends on individual surgical technique and experience

14. Are high risk groups of concern for efficacy or safety or both?

Expert #1	No
Expert #2	Not really.
Expert #3	PVP is safer than other BPH options in higher risk group cases, well documented in literature. And should not change efficacy.
Expert #4	I do not think so.
Expert #5	No
Expert #6	Safety is not a concern in the high risk groups Efficacy: Short/ Medium term outcomes are good and comparable to TURP (this applies to prostates upto 100g). For prostates> 100g, there is evidence supporting the use of GLL, however in contemporary clinical practice, we would discuss and offer (or refer) the patient an enucleation technique. Long term data is lacking.
Expert #7	Safety
Expert #8	It has been shown to be safe if used in experienced hands and efficacious in the short to medium term. Reintervention rates are however higher in the long term compared to other techniques like HoLEP.

15. Are patients on alpha-blockers considered high risk?

Expert #1	No
Expert #2	No

Expert #3	Not to my knowledge
Expert #4	No. Alpha blockers is the first line treatment (if conservative management fails) for symptomatic management of LUTS, before patients are offered surgery.
Expert #5	No
Expert #6	No
Expert #7	No
Expert #8	No

16. We understand preservation of sexual function is a key outcome of consideration for this population. Do you have any experience of positive or negative trends in this outcome with Greenlight XPS? How does it compare to other treatment options for this outcome?

Expert #1	In RCT's dry orgasm in 55% (TURP 65-80%, HoLEP 80-90%) New erectile dysfunction less than 1%
Expert #2	The likelihood of ED is 1-2% in my experience which is better than TURP. The risk of dry ejaculation is 30-50% and the technique can be adapted to reduce this further (it fairs better than HoLEP and TURP for this side effect).
Expert #3	There is no difference from standard TURP – however I noticed less incidence of ejaculatory dysfunction and no change to baseline erectile function, this will require further research support with longer tem studies.
Expert #4	I do not have any experience as I do not use this technology. I understand from colleagues that the PVP technique can be adjusted to improve chances of preservation of sexual (especially ejaculatory) function, although there is no guarantee.
Expert #5	I think the procedure is equal to TURP regarding the postoperative sexual function. I offer Rezum or Urolift for patients who particularly value preservation of both erections and antegrade ejaculation after a prostatic surgery.
Expert #6	Retrograde ejaculation is a known side effect of TURP in around 90% of patients. This is true of Greenlight laser vaporisation. I quote a similar incidence for this side-effect when counselling for GLLP. Impotence: 2-5% for TURP. Underlying physiology is not fully understood. There is a suggestion GLL might be slightly better for this, however I quote the same incidence for GLL and TURP.
Expert #7	Compared to HoLEP and TURP, probably not much different but certainly a greater risk than with Rezum and Urolift
Expert #8	Greenlight XPS has slightly higher depth of penetration compared to Holmium laser hence risk of erectile dysfunction may be slightly more but in practice there is little difference. Ejaculatory dysfunction is same as with any cavity producing procedure unless ejaculatory hood preserving procedure is considered, the efficacy of which is not yet well proven.

EQUALITY CONSIDERATIONS

17. The device IFU indicate it is contraindicated in individuals with prostate cancer. Has this prevented your patients receiving the care they require?

Expert #1	This is nonsense and we have published on its use in prostate cancer showing greatly improved outcomes and safety compared to previous TURP case series
Expert #2	No I am happy to offer to patients with prostate cancer.
Expert #3	I see no justification not to use green-light PVP in treating LUTs/urinary retention in cancer patient awaiting radiotherapy or on hormonal treatment but definitely not in cases awaiting radical prostatectomy.
Expert #4	There are good alternative options for prostate cancer patients, which also allow for retrieval of tissue that can be used for histological inspection (e.g. TURP or HoLEP), something that PVP technique does not provide.
Expert #5	I have performed GreenLight laser on patients with treated prostate cancer (after radiotherapy or hormonal manipulation) with good outcomes. I think IFU relates to the procedure being the treatment for prostate cancer.
Expert #6	No- we have offered GLL to prostate cancer patients except those who have received radiotherapy for prostate cancer previously.
Expert #7	No, these patients will be on a faster cancer pathway
Expert #8	This does not apply to ALL prostate cancer patients. Some patients with prostate cancer still may have an obstructing adenoma which can be treated by vaporisation or enucleation or resection.

18. In your experience how important is the absence of histological tissue examination in PVP when considering individual patient management?

Expert #1	No man should be diagnosed by TURP biopsy for a number of reasons. TP Biopsy can be carried out contemporaneously with GreenLight, and tissue can easily be removed using the laser if needed.
Expert #2	Not important. If we suspect prostate cancer pre-op we do an MRI. There is evidence to support this in the literature.
Expert #3	The current prostate cancer diagnostic pathways are mainly dependent on PSA/MRI followed by targeted biopsies – Most patients awaiting bladder outlet surgery will have both PSA and DRE as standard of care and if suspicious then MRI and biopsy will be the next step – the incidental finding of tumour cells in TURP chips is becoming less important with the new diagnostics pathways.
Expert #4	A small proportion of patients are found to have incidental prostate cancer on resecting or enucleating techniques (e.g. TURP or HoLEP). If the clinical suspicion for prostate cancer is low (i.e. low PSA, normal preoperative MRI prostate, normal prostate examination), histology is not so important. If there is a clinical suspicion, histology would be important.
Expert #5	I usually rule out prostate cancer in any patients who are listed for the procedure, so I do not think that the absence of the tissue specimen is of concern.

Expert #6	With the advent of multi-parametric MRI for prostate cancer diagnosis, the absence or presence of histological tissue examination has very little relevance in individual patient management.
Expert #7	Provided patients have had an appropriate assessment prior to surgery, this does not pose an issue.
Expert #8	It is a significantly important factor unless the patient has gone through investigations to exclude prostate cancer. Patients have an inherent anxiety to know if they have cancer with any urinary symptom and the lack of available tissue can elevate their anxiety.

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19. Are you aware of any patients who identify as female and have retained a prostate that have undergone treatment with Greenlight XPS for BPH? Would you have any concerns with using this technology in this population? Are there any surgical modifications or techniques that would be recommended in this population and are these within the Final Scope (e.g. accessing the tissue)?

Expert #1	I have treated two M-F GRS patients with no difference to natal male patients in any way, although ejaculatory dysfunction is rarely an issue in this group.
Expert #2	No
Expert #3	NA
Expert #4	I have no experience in this scenario. I can't think of a reason why the operation would be altered for this patient group, but again I have no experience in this.
Expert #5	I am not aware of such patients.
Expert #6	No change in technique or concerns in this patient population
Expert #7	*Are you aware of any patients who identify as female and have retained a prostate that have undergone treatment with Greenlight XPS for BPH*? No *Would you have any concerns with using this technology in this population?* No *Are there any surgical modifications or techniques that would be recommended in this population and are these within the Final Scope (e.g. accessing the tissue)?* No
Expert #8	I have no experience in this situation although I have seen such patients who did not require any intervention. The only concern is a short urethra and I presume power settings need to be carefully chosen in such cases.

ADVERSE INCIDENCTS

20. We understand there are issues with the fibre breaking and device malfunctions. Is this something you have experienced? Is there any risk to the patient or clinician when this occurs? Are there any other adverse incidents you are aware of with the Greenlight XPS system that we should be aware of?

Expert #1	Fibre breakage has occurred in about 1:400 cases, usually due to poor beginner technique or bad device placement (running a trolley over a laser fibre lying on the floor) One trainee had a small burn on the thumb. No visual risk if all in theatre wearing laser glasses.
Expert #2	This is rare No risks to patient or surgeon experienced. Sometimes if there is persistent bleeding - diathermy is required using electrocautery so when consenting patients I warn them of the potential risk of needing to use or switch to TURP/diathermy.
Expert #3	The only problem I had with fibers is mal-functioning and not firing as a safety measure from the generator with no serious incidents reported.
Expert #4	I have no personal experience in this. However, I have experience with using holmium laser for HoLEP. If the laser fibre breaks, it can be a risk to patients and theatre staff, depending what part of the fibre breaks (inside the scope, outside the scope), whether the laser is firing at the time is breaks, and how early this is recognised. I have not heard of any incidents.
Expert #5	I have experienced machine malfunction on one or two occasions after 5 years of use. I usually consent the patients to conversion to TURP if it does happen. The fibre breakage occasionally happens (as above).
Expert #6	Fibre malfunction has occurred in occlusive prostates due to tissue contact when using the laser. The Moxy fibre has inbuilt sensor which puts the laser in standby mode as a safety measure. Also, you would notice that the direction of the aiming beam of the laser has altered when the fibre tip has been damaged at which point the fibre has to be replaced. I am not aware of any fibre breaking or adverse events causing staff or clinical hazards. There is a potential risk to patients if one would continue to operate despite a distorted / mis-firing aiming beam.
Expert #7	*We understand there are issues with the fibre breaking and device malfunctions. Is this something you have experienced?* No *Is there any risk to the patient or clinician when this occurs? Are there any other adverse incidents you are aware of with the Greenlight XPS system that we should be aware of?*

	No
Expert #8	I have not faced any such incident personally but I think if all laser safety precautions are followed not only by the surgeon but the whole theatre team adverse events are avoidable

Please do add any further comments about your experience of Greenlight XPS:

Expert #1	No additional comments
Expert #2	If there a multiple small stones in the prostate cavity this can damage the laser fibre – it is rare but another reason for having to switch to TURP, or if the anatomy is difficult – care has to be taken when lasing close to the ureteric orifices.
Expert #3	No additional comments
Expert #4	No additional comments
Expert #5	No additional comments
Expert #6	I have initiated and set up a Yorkshire Greenlight users group recently- in the Yorkshire and Humber region there are 5 centres using this technology. The aim of getting together was to share our experience of using GLL, offer peer support and training, collaborate data for outcomes and to maintain our continuing professional development relating to this procedure and the other newer technologies for BPH. I would like to summarise that • GLLP can replace TURP (for prostates up to 100g) • Can be carried out as a day case • Less incidence of re-admissions to hospital due to secondary haemorrhage • Safe (safer) in patients on anticoagulants/ anti-platelets agents • Similar efficacy (to TURP) in patients with retention (I am in the process of collating Yorkshire regional data to show real life NHS outcomes) • Some role in prostates >100g, will depend on experience on the surgeon and usually applied in selected cases.
Expert #7	No additional comments
Expert #8	No additional comments

Thank you very much for your time and expertise

Appendix 5

Additional question sent to clinical experts and Company 02/12/2021

1. Is “ejaculatory hood sparing GreenLight Laser prostate photoselective vaporization” considered the same as anatomical vaporisation, and in scope?

Expert #1	Richard Hindley
Expert #2	Gordon Muir
Expert #3	Marios Hadjipavlou
Expert #4	Andrew Thomas
Expert #5	Feras Al Jaafari
Expert #6	Aniruddha Chakravarti
Expert #7	Amr Emara
Expert #8	Glyn Burtt (Company’s Medical Director)

Collated responses

Expert #1	Anatomical PVP is essentially getting down to the prostate capsule using a particular technique and it creates a TURP like cavity. Ejaculatory sparing can be done simultaneously with this but it is about preserving some apical tissue so as to try and direct the ejaculate in the correct direction. The verumontanum and the seminal colliculus are preserved. With a TURP or HoLEP this area is usually disrupted. The down side is that it may be associated with a slightly higher retreatment rate as not quite as much tissue is removed. On the positive side the likelihood of incontinence and dry ejaculation is reduced.
Expert #2	It's a minor variation of the standard operation which leaves some tissue at the tip.of the prostate. This reduce risk of dry organs from 60% to 13% Outcomes same as standard vaporisation
Expert #3	Yes - this is within scope. I believe it is a minor surgical technique modification to attempt preservation of ejaculatory function.
Expert #4	No this is different. First procedure is to try and preserve ejaculation post-surgery . Anatomical is a variant of a technique in performing the procedure.
Expert #5	Excellent question - which shows a good dissection of the evidence! Anatomical Photoselective Vaporisation of the Prostate (PVP) is an advanced technique for vaporisation - introduced by Fernando Gomez Sancha where the prostate is vapo-enucleated after identifying anatomical landmarks. While ejaculatory sparing Greenlight is a modified procedure where the authors tried to spare ejaculation by preserving 1 cm of tissue in front of the veru-

montanum (anatomical landmark in the prostatic cavity). It is not an established approach but looks very promising.

I am happy to talk over the phone if more information is required as this topic is actually very interesting.

Here I attach two papers that describe ejaculation sparing PVP and a link for anatomic PVP video publication (below):

Enrique Rijo and Fernando Gomez-Sancha.Videourology.Aug 2018.http://doi.org/10.1089/vid.2017.0054
https://www.liebertpub.com/doi/abs/10.1089/vid.2017.0054

The Evolution of Green Laser (532 nm) Techniques in the Treatment of Benign Prostatic Obstruction: Not Only for Photoselective Vaporization of the Prostate | Videourology

Abstract Introduction: The first human trials with the 60 W green laser (KTP/532 nm) used in the treatment of lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) were conducted in 1998. The term “photoselective vaporization of the prostate” (PVP) was introduced by Professor Reza Malek. PVP is an established, safe, and effective alternative to transurethral resection of the

	prostate for the treatment of BPH obstruction. Nowadays the majority of urologists are unaware of other approaches and techniques with green laser, apart from PVP. Objectives: To demonstrate the evolution of techniques for the treatment of benign prostatic obstruction with green laser (532 nm) and to summarize the advantages and disadvantages of each technique. Materials and Methods: We review the main techniques for the treatment of LUTS secondary to BPH with green laser (532 nm), highlighting the advantages and disadvantages of each technique. Results: For the past 20 years, green laser technolo www.liebertpub.com
Expert #6	Ejaculatory hood preserving vaporisation or enucleation of prostate is a relatively new concept where about 1cm tissue around the verumontanum is preserved which is presumed to be responsible to aid antegrade ejaculation. The evidence from RCT or real-world studies are not strong enough yet to support this concept, but they are encouragingly positive. Very few patients were included so the concept is not yet conclusively proven. Anatomical enucleation or vaporisation, on the other hand, enucleates or ablates all apical tissue, not preserving any tissue around verumontanum. This is certainly more likely to cause retrograde ejaculation. I hope I have been able to answer your question but please don't hesitate to contact me if you have any further questions.
Expert #7	Ejaculatory hood sparing is a modification of any vaporisation technique to minimize risk of ejaculatory dysfunction and not the same as anatomical vaporisation
Expert #8	Ejaculatory hood sparing PVP is a minor technique modification to be very careful around the ejaculatory ducts as they enter the prostate at the verumontanum, with the goal to preserve antegrade ejaculation. The removal of prostate tissue to treat the underlying BPH is conventionally performed (standard PVP) or modified (anatomical

	vaporization), but anatomical and standard PVP should be within scope, as should the minor modification of these techniques in an effort to preserve antegrade ejaculation.

Appendix 6

Collated comments table

MTG Medtech Guidance:

Expert contact details and declarations of interest:

Expert #1	ANIRUDDHA CHAKRAVARTI, CONSULTANT UROLOGICAL SURGEON, THE ROYAL WOLVERHAMPTON HOSPITALS NHS TRUST, [redacted]
	Nominated by: NICE
	DOI: Provided expert opinion on Urolift procedure
Expert #2	Marios Hadjipavlou, Consultant Urological Surgeon, Guy's & St Thomas' NHS Foundation Trust, [redacted]
	Nominated by: NICE
	DOI: none
Expert #3	Maya Harris, Consultant Urological Surgeon, South Warwickshire NHS Foundation Trust, [redacted]
	Nominated by: NICE
	DOI: none
Expert #4	Ian Pearce, Consultant Urological surgeon, Manchester University NHS Foundation Trust, [redacted]
	Nominated by: NICE
	DOI: none
Expert #5	Mr Amr Emara, Consultant Urologist, Hampshire Hospitals Foundation Trust, [redacted]
	Nominated by: company
	DOI: none
Expert #6	Gordon Muir, Consultant Urologist, King's College and London Bridge Hospitals, [redacted]
	Nominated by: NICE and company
	DOI: 2009 - present : Mentor and consultant BSCI; 2018 – present: Mentor and consultant Olympus GMBH; 2013-2019 – present: Mentor and consultant Neotract

Expert #7	Mr Feras Al Jaafari, Consultant Urologist, NHS Fife, [redacted]
	Nominated by: BAUS
	DOI: Since 2017: I have been consulted (and paid) by the manufacturer (Boston Scientific) regarding this technology. I have given talks on patient centric approach in BPH sponsored by the company. Since 2018: I am a paid proctor in this procedure. I train other urologists in performing the procedure. Since 2021: I have visitors attending my theatre lists for which preceptorship fees are paid to the department.
Expert #8	James Andrew Thomas, Consultant Urological Surgeon, CTM UHB, [redacted]
	Nominated by: NICE
	DOI: none
Expert #9	Richard Hindley, Consultant Urologist, Clinical Lead for Urology and Visiting Professor, Hampshire Hospitals NHS FT, [redacted]
	Nominated by: n/a
	DOI: From approx. 2010: I do receive ad hoc payments as a clinical advisor and proctor for Boston Scientific; I was involved with the GOLIATH trial
Expert #10	Professor Iqbal Shergill, Consultant Urological Surgeon, Wrexham Maelor Hospital, [redacted]
	Nominated by: n/a
	DOI: none
Expert #11	Sanjay Rajpal, Consultant Urologist, Sheffield Teaching Hospitals, [redacted]
	Nominated by: company
	DOI: 29/09/21 I have received payment for proctoring services from Boston Scientific (manufacturer of the GreenLight XPS)

			Response
1	Please describe your level of experience with the procedure/technology, for example: Are you familiar with the procedure/technology? Have you used it or are you currently using it? Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake? Is this procedure/technology performed/used by clinicians in specialities other than your own? – If your specialty is involved in patient selection or referral to another specialty for this procedure/technology, please indicate your experience with it.	Expert #1 yes Used it, not currently using Still used in the NHS although not as widely as before Not known to be used in specialties other than urology This is a procedure to treat BPH used by urologists	
		Expert #2 I have undergone training for this procedure, however I have never performed this myself. It is not offered in my Trust, although it is offered in a nearby hospital within our regional Network (King's College Hospital), where it has been very well established for several years. According to the recent BAUS audit, Greenlight comprises 6.1% of all bladder outflow obstruction surgical procedures (https://www.baus.org.uk/_userfiles/pages//files/professionals/research//BAUS%20Bladder%20Outflow%20Obstruction%20National%20Report%20November%202020.pdf) To the best of my knowledge, Greenlight for benign prostatic hyperplasia is only performed by urological surgeons.	

		Selection for this procedure is decided by the urologist and the patient himself. Anaesthetic input may sometimes be required to assess for fitness (for example, if a patient is deemed by the surgeon and the anaesthetist unfit for general or spinal anaesthesia, prostate artery embolization or Rezum or Urolift may be offered instead).	
		Expert #3 I am very familiar with the Green Light Laser prostatectomy and performed about 200 procedures both in NHS and private sector since learning the procedure with a proctor in 2015. I do currently use it as a part of a portfolio of the procedures I offer for BPH, which also includes TURP, Rezum and Urolift. I am aware of the other centres in the region and in the country which perform the procedure routinely. It is not performed by clinicians of other specialities. Not applicable as above.	
		Expert #4 I am familiar with the technology I have not used the technology and am not aware of how widely this is used in the UK No My specialty is involved in counselling patients and selecting patients for this procedure	

		Expert #5 - I am very familiar with Green-Light Vaporisation of prostate procedure - I routinely use this technique in my daily practice for the past 10 years. - This procedure is adapted by few urology NHS centres across the UK, I think the technique safety and ease of use should qualify adopting the technique in many more centres. - I am not aware that Green-light is currently used by other specialities as routine. - I have substantial experience is using green-light PVP; both technically and on research front with previous publication of our local experience, I will be comfortable to advise on selection and referral criteria.	
		Expert #6 Subspecialist LUTS BPH surgeon, teacher, researcher	
		Expert #7 - I am very familiar with this procedure. I have been involved in >500 Greenlight laser procedures over the last few years and have	

		run multiple hands-on training courses teaching t to trainees and fellow consultants. - I am currently using it - On the recent BAUS snapshot audit the uptake is 6.1% across the UK (although this was only across one month – I suspect the uptake is over 10-15% - It is only used in urology and only to treat enlarged prostates	
		Expert #8 I have been using Greenlight laser technology since its inception in 2006. I was the Co Primary investigator in the Goliath Studies and led the initial application for NICE approval 5-6 years ago. I use the technology routinely as my primary operation for BPH in the NHS and private sector. There is a widespread use within the NHS – though it maybe patchy in some regions. no I have 15 years experience and have taught this technique across various centres in UK, Europe and the USA.	
		Expert #9 Familiar – I have been using this technology since 2005 as a Consultant having trained in its use in 2003. I have performed over 1500 cases.	

		I am still using it regularly performing 1-2 cases per week There was guidance in 2016 which I was involved with – adoption advice. It is relatively underutilised in the UK. No.	
		Expert #10 Familiar with technology. Not used it or currently using it. Aware of centres in NHS using this technology. Not used elsewhere. N/A	
		Expert #11 I am currently using this technology In addition to my centre, 4 other units in the region (Yorkshire & Humber) use this technology Uptake for this technology is increasing particularly since GIRFT recommendations and with the pressures on hospital beds and the attraction of carrying out this procedure as a day case This technology is only used in urology	
2		Expert #1 I have done bibliographic research on this procedure.	

	− Please indicate your research experience relating to this procedure (please choose one or more if relevant):	Other (please comment)	
		Expert #2 I have had no involvement in formal research on this procedure. However, I have previously provided expert opinion on this procedure to NICE, which involved some literature research.	
		Expert #3 I have done bibliographic research on this procedure and follow any publications which appear in the relation to it.	
		Expert #4 I have had no involvement in research on this procedure.	
		Expert #5 I have done clinical research on this procedure involving patients or healthy volunteers. I have published this research.	
		Expert #6 I have done bibliographic research on this procedure. I have done research on this procedure in laboratory settings (e.g. device-related research). I have done clinical research on this procedure involving patients or healthy volunteers. I have published this research.	

		ALL OF the above	
		Expert #7 I have published (co-authored papers on this topic) Trail, M., Good, D., Clyde, D., Brodie, K., Leung, S., Simpson, H., Kata, S. G., Tsafrakidis, P., Chapman, R. A., Mitchell, I., Janjua, K., & Al Jaafari, F. (2021). Day Case GreenLight Laser Photoselective Vaporisation of the Prostate (GL-PVP): Evaluation of Outcomes from a District General Hospital Experience of 538 Cases. *Journal of Endoluminal Endourology*, *4*(3), e8-e16. https://doi.org/10.22374/jeleu.v4i3.128 Trail, M., Hindley, R. G., **Al Jaafari, F**. (2021). Contemporary surgical management of benign prostatic obstruction: does there remain a place in the toolbox for TURP? *Journal of Clinical Urology*. https://doi.org/10.1177/20514158211010646 Johnston MJ, Guillaumier S, **Al Jaafari F**, Hindley RG (2019) The Urological Stethoscope: An essential aide for the modern BPH Specialist? BJUI 2020 May;125(5):632-633 doi: 10.1111/bju.14979. Epub 2020 Jan 8.	

		Expert #8 I have done bibliographic research on this procedure. I have done clinical research on this procedure involving patients or healthy volunteers. I have published this research. (Alex Bachmann and myself were lead authors / investigators in GOLIATH study) Other (please comment)	
		Expert #9 I have done bibliographic research on this procedure. Yes I have done research on this procedure in laboratory settings (e.g. device-related research). No I have done clinical research on this procedure involving patients or healthy volunteers. Yes We were a centre in the GOLIATH study.	
		Expert #10 I have had no involvement in research on this procedure. Other (please comment)	
		Expert #11 I have no involvement in research on this procedure.	

Current management

3	How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design? Which of the following best describes the procedure (please choose one):	Expert #1 Used since a long time. Ablative procedure, not new, not novel approach Established practice and no longer new.	
		Expert #2 Established practice and no longer new.	
		Expert #3 Green light laser prostatectomy is innovative compared to the TURP (standard). It causes less bleeding and has easier postoperative recovery. It has been developed 10-15 years ago. Established practice and no longer new.	
		Expert #4 This represents a new technology utilised to perform a well performed procedure, as such it represents a moderate variation Established practice and no longer new.	
		Expert #5 Established practice and no longer new.	
		Expert #6 Established practice and no longer new.	
		Expert #7	

		Established practice and no longer new.	
		Expert #8 Safer and equally effective to TURP (Goliath data) Established practice and no longer new.	
		Expert #9 Novel – uses the unique characteristics of the greenlight wavelength to selectively vaporise vascular tissue. Established practice and no longer new. There are adaptations and new ways of using the technology – for example, it can be used to enucleate. The technique I sue predominantly is that of anatomical vaporisation – using the technology for what it was designed – photoselective vaporsation down to the prostate capsule to create a TURP like cavity but with a better safety profile.	
		Expert #10 Established practice and no longer new.	
		Expert #11 This procedure is a relatively novel approach when compared to current standard of care Established practice and no longer new.	
4	Does this procedure/technology have the potential to replace current standard care or	Expert #1 Addition to other standards of care	

	would it be used as an addition to existing standard care?	Expert #2 To be used in addition to alternative treatment options for BPH.	
		Expert #3 I think the technology should be offered as a part of the portfolio of the procedures for BPH. I use TURP if histology of prostatic tissue is important for the patient, or Rezum procedure if the patient wishes to preserve ejaculation.	
		Expert #4 Used as an optional variation in care	
		Expert #5 In a stepwise approach it can be implemented more widely to prepare for future replacing of current less safe (with higher risk of complications) standard of care.	
		Expert #6 Yes and it should	
		Expert #7 Yes- it has the potential to replace the current standard of care due to its higher safety profile	
		Expert #8 Yes – replace	
		Expert #9	

		Could replace – perhaps in combination with other procedures that have a better safety profile than TURP such as HoLEP and the minimally invasive procedures Rezum and Urolift.	
		Expert #10 Used in addition	
		Expert #11 Potential to replace the current standard of care	

Potential patient benefits

5	Please describe the current standard of care that is used in the NHS.	Expert #1 TURP, Urolift, HoLEP, Rezum, Green light laser ablation	
		Expert #2 Several treatment options are available for management of BPH. If there is indication for surgical intervention, the options offered are: transurethral resection of the prostate (TURP – can be bipolar or monopolar), Holmium laser enucleation of Prostate (HoLEP), Urolift, Rezum, or Prostate Artery Embolization. They have a different side effect profile and they are indicated for different sizes of prostates. The options are therefore discussed and agreed with each patient.	
		Expert #3	

		BAUS Bladder Outlet Obstruction audit (2019) has demonstrated that TURP (both monopolar and bipolar) is the leading procedure and Green Light laser prostatectomy was used in 6.1% of cases.	
		Expert #4 Current standard of care for outflow surgery is now variable with multiple options being available and offered including 1. TURP 2. Bipolar TURP 3. Urolift 4. HoLEP 5. Rezum 6. Prostate artery embolisation	
		Expert #5 Transurethral resection of prostate either Monopolar or Bipolar is the current standard of care in nearly 80% of UK centres with the remaining using laser technique as supplementary.	
		Expert #6 Variable depending on local expertise and prejudices	
		Expert #7 The BAUS snapshot audit showed that TURP was used in the treatment of 60.5% of all patients requiring bladder outflow obstruction surgery.	

		Expert #8 My practice – Green light laser followed by TURIS (bipolar TURP – second choice)	
		Expert #9 The conventional standard of care has been TURP for the majority. This is no longer the case in my opinion. I am Chair of the BOO GIRFT Academy and the document we are working on is nearly complete – we feel that the new gold standard is to have a portfolio of treatment options. BAUS our national organisation are in agreement with this principle. No one procedure treats all anymore as we need to be patient centric rather.	
		Expert #10 Monopolar TURP	
		Expert #11 TURP (monopolar and bipolar) is currently the most commonly performed bladder outflow surgical procedure in the NHS	
6	Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this? If so, how do these differ from the procedure/technology described in the briefing?	Expert #1 Aquablation	
		Expert #2 The options mentioned above form the alternatives, and they have different indications and contraindications as well as different side	

		effect profiles, which are well documented in the literature.	
		Expert #3 The competing procedures are TURP, Rezum, HOLEP, PAE, Aquablation and Urolift. All of these procedures could be used for treatment of BPH, depending on prostate volume, presence of urinary retention, patient's preference and local availability.	
		Expert #4 The alternatives are as above They employ a different mechanism TURP involves the use of heat (current) to remove prostatic tissue Urolift utilises surgical implants to compress and pin back the prostatic tissue Rezum involves injections of steam into the prostate resulting in cell death PAE involves occluding the main blood supply to the prostate resulting in cell death and shrinkage	
		Expert #5 There is more than one laser technology used in the BPH market, targeting less bleeding risk with shorter hospital stay and robust out-comes, but according to current evidence Green-Light PVP is one of the safest modalities.	

		Expert #6 HoLEP, REZUM, ITIND, Urolift All capable of outperforming TURP in terms of bed usage and recovery for selected patients in some cases. Both lasers equivalent to or better than TURP but safer.	
		Expert #7 No other vaporising technique competes with Greenlight laser from a mode of action point of view. There are other novel technologies with different mode of action that are NICE approved we lack long term data regarding durability (Urolift, Rezum)	
		Expert #8 Holmium enucleation of prostate	
		Expert #9 No – Greenlight is very good for patients with a bleeding tendency and overall has a very good safety profile.	
		Expert #10 Bipolar Vaporisation – different in sense of different energy source used e.g.: electric current rather than laser.	
		Expert #11	

		1. Holmium laser Enucleation of Prostate (HOLEP) - this is a different type of laser which is used for the same problem. This procedure is enucleation of the prostate whereas the Greenlight laser involves photo-selective vaporisation of the prostate. HOLEP has a greater learning curve, involves overnight stay and will need additional equipment like a morcellator. HOLEP procedure is very useful for patients with large prostates (100cc+) 2. Transurethral vaporisation of the prostate (TUVP): This technology results in electro-vaporisation of the prostate. A modification of the loop in TURP is used and the prostate tissue is treated resulting in a cavity similar to TURP and GLLP 3. Thullium Laser vaporesection of prostate (ThuVARP): Thullium laser can be used to remove the obstruction in the prostatic urethra using principles of vaporisation and nucleation. Currently available in a very few centres in the UK. Non-inferiority to TURP has been shown in studies.	
7	What do you consider to be the potential benefits to patients from using this procedure/technology?	Expert #1 Choice of an alternative procedure towards surgical treatment of bladder outflow obstruction	
		Expert #2 The main advantages of this technology over other BPH procedures such as TURP, is the haemostatic property of laser, which means that an anticoagulated patient may not need to stop their medication for the operation. Also this	

		procedure can be performed as day surgery, as opposed to TURP or HoLEP which typically require 1-2 nights inpatient stay. It is also considered a less difficult procedure to learn compared to alternatives such as HoLEP or possibly TURP.	
		Expert #3 The benefits of Green Light laser include reduced bleeding and need for postoperative bladder irrigation with subsequent earlier discharge and easier postoperative recovery.	
		Expert #4 Lower blood loss compared to standard TURP Fewer complications Shorter hospital stay	
		Expert #5 Safe / less risk of bleeding/ no TUR syndrome risk - and accordingly risk of re-hospitalisation and need for blood-transfusion will be significantly less compared to standard technique – eventually leading to overall less hospital nights.	
		Expert #6 Faster recovery better use of resources	
		Expert #7 Higher safety profile than TURP. Can be performed as a true daycase. Less bleeding.	

		Shorter surgical time. Long term data available in the literature.	
		Expert #8 Safety / day case procedure / return to normal health quicker than the standard of care in NHS	
		Expert #9 Good safety profile / reduced risk of bleeding/ no TUR syndrome risk - and accordingly risk of re-hospitalisation and need for blood-transfusion will be significantly less compared to standard technique. A reliable daycase procedure. No requirement for any irrigation post procedure in 99%.	
		Expert #10 Less bleeding risk and hence can be potentially used as daycase surgery especially in patients on anti-coagulants which are high risk patients.	
		Expert #11 1. Less blood loss- safer in patients on anti-platelet and anticoagulant medications and the general population as there will be less physiological strain 2. Reduced risk of secondary haemorrhage – resulting in less use of healthcare resources post-operatively (as the laser is very haemostatic) 3. Can be done as day case 4. Similar outcomes to TURP	

Potential system impact

8	Are there any groups of patients who would particularly benefit from using this procedure/technology?	Expert #1 Patients needing a short procedure with ablative therapy to treat bladder outflow obstruction from a small to medium sized prostatic adenoma with no need for histological analysis of tissue	
		Expert #2 As mentioned above, patients on anticoagulants that is best to avoid stopping may be more suitable for Greenlight PVP than any of the other options.	
		Expert #3 Elderly patients, especially on anticoagulation	
		Expert #4 Men with symptoms from bladder outflow obstruction caused by prostatic enlargement who wish a more long term proven surgical resolution	
		Expert #5 Older patients and patients with higher risk of bleeding or on anti-coagulation. And this is the wider range of patients requiring this procedure.	
		Expert #6	

		High risk, anticoagulated, patients with implantable devices, patients who enjoy sex	
		Expert #7 High risk patients – catheterised, on anticoagulants, co-morbid (ASA III, IV)	
		Expert #8 Elderly / those anti-coagulated / larger prostate volumes	
		Expert #9 Older patients and patients with higher risk of bleeding or on anti-coagulation.	
		Expert #10 As above	
		Expert #11 1. Patients who are on anticoagulants/ anti-platelets agents 2. Most patients who need a TURP might be benefitted by this	
9	Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system? Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?	Expert #1 I do not think so No	
		Expert #2 This procedure can be performed as day surgery, as opposed to TURP or HoLEP. The functional outcomes are comparable with that of TURP, which is slightly more invasive with a	

		higher risk of bleeding perioperatively, although not very significant nowadays with bipolar TURP.	
		Expert #3 It does lead to the reduced hospital stay, less invasive treatment, less need for postoperative blood transfusion, easier recovery with less visits.	
		Expert #4 Shorter hospital stay	
		Expert #5 Yes, less risk or re-hospitalisation, less burden on blood banks (hardly any requirement for blood transfusion with no need for routine group & save), many cases can be a day case procedure and eventually shorter hospitalisation.	
		Expert #6 Potential to abolish over 90% of overnight stays for men with LUTS BPH including urinary retention	
		Expert #7 Yes, especially in the peri/post-COVID recovery era. Patients will not require an inpatient bed as they can be done as a true daycase. If the patient gets admitted, they are usually discharged the following morning. This is crucial given the bed pressures in the NHS. The functional outcomes are equivalent to TURP in the long term.	

		Expert #8 It has already in my practice Yes and yes	
		Expert #9 Yes, no inpatient bed required. Reduced bleeding risk. Good procedure for those with higher ASA scores. Yes	
		Expert #10 Potentially less hospital stay. Functional outcomes likely to be similar though.	
		Expert #11 Yes – in my centre, we were doing TURP previously with average length of stay being 3.2 days. Since starting Green light laser in 2018, 62% of these patients are done as day case. The remaining 38% patients stay in overnight mainly due to social, general frailty reasons. Outcomes studies so far suggested-1. Reduced LOS 2. Efficacy similar to TURP 3. Reduced re-admission rates with post op complications. It is a less invasive treatment compared to TURP	
10	Considering the care pathway as a whole, including initial capital and possible future	Expert #1 About the same	

	costs avoided, is the procedure/technology likely to cost more or less than current standard care, or about the same? (in terms of staff, equipment, care setting etc)	Expert #2 I am not aware of the financial aspects around Greenlight.	
		Expert #3 I think the cost is similar to TURP.	
		Expert #4 Probably less	
		Expert #5 Overall factoring the re-hospitalisation and inpatients nights. This proven to be a cost-effective procedure compared to current standard of care.	
		Expert #6 A bit less	
		Expert #7 • Yes, the procedure will have potential cost savings • As per the NICE document in 2016 - “NICE's resource impact report estimates that the annual cost saving for the NHS in England is around £2.3 million. In a plausible scenario of 70% of treatments being done as day cases, the cost saving may be up to £3.2 million.”	

		Expert #8 Last nice assessment – from memory – if greenlight replaced every TURP in NHS – saves £167 per case	
		Expert #9 Less by £500 approx. when compared to TURP as per previous data.	
		Expert #10 More costly, as laser fibres will be more expensive than loops used in monopolar TURP.	
		Expert #11 This procedure should cost less (or cost equal) than the current standard of care	
11	What do you consider to be the resource impact from adopting this procedure/technology (is it likely to cost more or less than standard care, or about same-in terms of staff, equipment, and care setting)?	Expert #1 Cost of fibres could be balanced by shorter length of stay	
		Expert #2 I am unable to comment on cost-related questions. In terms of equipment, this technology requires on a capital investment on the laser device/generator and then consumables. It also required to be performed in laser-safe theatres (which may require specific installations), a high energy socket, and theatre staff laser and procedure-specific training.	
		Expert #3	

		I think it is cost-neutral with higher outlay for the laser fibre and reduced costs due to reduced hospital stay and less intensive nursing required.	
		Expert #4 High initial cost for the equipment Ongoing costs re maintenance contracts	
		Expert #5 As expected, there will be initial capital investment to introduce the service, but this will be automatically diluted with less inpatient nights and less risk of post-operative complications with no need for transfusion or using critical care beds.	
		Expert #6 A bit less	
		Expert #7 Cost saving Safer procedure/ less bleeding Shorter hospital stay Shorter surgical time	
		Expert #8 You need to buy new equipment initially- laser and adapt your resectoscopes	
		Expert #9	

		Less than standard of care. The cost of a TWOC is more than off set by the absence of a requirement for blood transfusion, reduced bed stay and lower risk of side effects requiring treatment such as ED and strictures.	
		Expert #10 Similar resources.	
		Expert #11 This procedure should cost less (or cost equal) than the current standard of care	
12	What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?	Expert #1 Laser safe theatre	
		Expert #2 Laser-safe theatre (e.g. laser curtains, laser-safety goggles, etc) and laser-certified theatre staff.	
		Expert #3 Laser machine (with fibres and glasses), laser-safe theatre, staff training	
		Expert #4 Laser training Protective eye wear	
		Expert #5 Laser safe operating theatre with the relative personnel training are required for using this technology	

		Expert #6 none	
		Expert #7 Laser proofing of the operating theatre (most urology theatres are laser proofed). The purchase of the laser machine (the company can place it otherwise on a fibre consumption contract). Staff need to be trained.	
		Expert #8 Anaesthesia – GA or spinal and a day case theatre	
		Expert #9 Laser safe theatre.	
		Expert #10 Laser compatible theatres. Laser trained staff.	
		Expert #11 1. Theatres: should be made laser safe as per standard guidelines. 2. Power socket for laser will be needed 3. Equipment : Minor change to the existing TURP kit will be needed like the beak of the sheath will need changing to metal beak and a separate laser bridge will need to be procured 4. Laser safety glasses 5. Capacity for day case surgery and post procedure clinic slots for catheter removal will need to be factored in	

		6. Surgeon and theatre staff training	

General advice

13	Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?	Expert #1 Staff needs laser safety training, operator needs to be trained, surgeon needs training to do the procedure	
		Expert #2 Yes – laser safety certification, as well as training specific to the use of this device. These can usually be arranged and organised by the company.	
		Expert #3 Laser training for the staff with the dedicated laser operator in the theatre during the procedure.	
		Expert #4 Yes, laser safety training for all staff	
		Expert #5	

		Yes – The standard laser safety course is mandatory requirement plus the expected technique training that is currently provided through the relative courses or in many centres as part of specialty training program.	
		Expert #6 Validated simulator and mentorship programmes exist	
		Expert #7 Core laser knowledge course and basic laser handling training (transferrable from other existing laser knowledge skills).	
		Expert #8 Yes	
		Expert #9 Yes – training as per company standard which includes simulator training and proctoring of initial cases.	
		Expert #10 As above.	
		Expert #11 Yes- Laser safety course (run by the manufacturer), simulator training and hand on training with a proctor (provided and supported by the manufacturer)	

Other considerations

14	What are the potential harms of the procedure/technology? Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence: Adverse events reported in the literature (if possible, please cite literature) Anecdotal adverse events (known from experience) Theoretical adverse events	Expert #1 No histology available Powerful laser - needs to be handled with care by adequately trained staff Bleeding, secondary haemorrhage	
		Expert #2 This technology has been well tested over several years and is generally considered a safe procedure, when performed by appropriately trained staff. The XPS (180W) should be evaluated separately from the older model (120W) which was less powerful, therefore considered slower and less effective and appropriate for very large prostate glands. Anecdotally, I have heard from colleagues that a significant proportion of patients will suffer from dysuria, urethral discomfort, urgency and frequency, due to sloughing of the tissue from the prostatic cavity (when compared to the other BPH treatment options). However, although relatively common, this is not considered a major side effect and usually improves with time or with the use of non-steroidal anti-inflammatory drugs. Injury to the ureteric orifices by the laser has also been reported, which can lead to severe	

		complications requiring surgical intervention (ureteric strictures). As with most BPH procedures (except perhaps HoLEP), there is prostate regrowth over years and there is therefore a reintervention rate associated with Greenlight.	
		Expert #3 The authors below quote bladder neck stenosis in 1%, but also I counsel the patients preoperatively that the procedure could cause haematuria, infection (UTI), retrograde ejaculation in the majority of cases, incontinence (serious in about 1%), erectile difficulties.	
		Expert #4 Recurrence Stricture Erectile dysfunction	
		Expert #5 As any Laser technology, respecting the standard safety requirement will keep it safe to use. Using the necessary protective equipment and having a laser officer in theatre is mandatory part of using this technology to keep it safe. Adverse events: bleeding necessitating transfusion (<1%) - Retrograde ejaculation (50-60%), risk of infection (2 -5%), Risk of scarring (urethral stricture/ Bladder neck stenosis – 1-	

		2%) - Need for re-do (3-7%) - Incontinence (<1%)	
		Expert #6 As with all LUTS BPH procedures, but less common	
		Expert #7 Any surgical procedure carries some risks – Bleeding – requiring transfusion <1% Stricture – 2-5% Retreatment – up to 10-15% in 10 years Impotence <1% Retrograde ejaculation 50-70%	
		Expert #8 Sane as TURP – UTI / bladder neck scarring UTI – 5%, retrograde ejaculation 66% / bleeding – rare <1% n/a n/a – just read the papers from Goliath papers – top quality studies – answers all these questions	
		Expert #9 Reduced complication rates when compared with TURP (GOLIATH Trial).	

		ED 1-2% dry ejaculation 30-50% Incontinence < 1% Transfusion 0%	
		Expert #10 Potentially high rates of patients needing re-do surgery in future.	
		Expert #11 Procedure specific: Dysuria, Urinary tract Infection, Sepsis, Bleeding (risk of transfusion<1%), Retrograde ejaculation (70-90%), Impotence(1-2%), Transient incontinence (5%), Bladder neck stenosis (5%), urethral stenosis (1-5%), Adjacent organ injury(ureteric/ bladder injury)<1%, No tissue for histology, Failure to void, Re-operation rate (slightly higher than TURP) Risks from anaesthesia and hospitalisation including DVT, PE From experience: Sepsis necessitating ITU stay and further complicated by leg ischaemia needing embolectomy, cardiac arrest intra-operatively followed by subsequent demise, dystrophic calcification (in patients (x3) who had previous prostate radiotherapy) necessitating trans-urethral resection of the calcification in the prostatic urethra	
15	Please list the key efficacy outcomes for this procedure/technology?	Expert #1 Persistent relief of symptoms in a safe and effective way with minimal complications	

		Expert #2 Perioperative – inpatient stay / intraoperative complications / successful trial without catheter Long-term – catheter-free rate / IPSS score / reintervention rate	
		Expert #3 Mean IPSS nadir was reached at three years, with a drop of 80.4% (−21.1 points). Similarly, mean quality of life (QoL) score dropped by 82.8% after three years (preoperative mean of 4.7). With respect to mean Qmax, there was an increase by 72.7% (+14.7 mL/s) at one year, reaching the value of 19.9 mL/s. Moreover, mean PVR was 32.8 mL at four years compared to 345 mL preoperatively. [Kevin C. Zorn et all. Photoselective vaporization of the prostate with the 180-W XPS-Greenlight laser: Five-year experience of safety, efficiency, and functional outcomes. Can Urol Assoc J. 2018 Jul; 12(7): E318–E324.]	
		Expert #4 IPSS score Complication rate Length of stay Reoperation rate	
		Expert #5 Safely managing bladder outlet obstruction symptoms and urinary retention with significantly improve in patient’s quality of life.	

		Expert #6 IPSS scores, catheter free retention outcomes	
		Expert #7 Improvement in flow, post void residual, IPSS score, QoL scores and successful trials without catheter (for catheterised patients)	
		Expert #8 Improvement in IPSS, Qol, QMax on a flow rate / catheter free rate if patient is in retention	
		Expert #9 2-5 year retreatment rates, PROMS's, complication rates	
		Expert #10 Symptom improvement during clinical follow up – measured with IPSS.	
		Expert #11 1. Improvement in IPSS scores and Qmax 2. Day case rates 3. Successful TWOC rates in patient treated for urinary retention 4. Re-operation rates (long term-i.e.>36 months)	
16	Please list any uncertainties or concerns about the efficacy and safety of this procedure/?	Expert #1 Risk of sexual dysfunction and incontinence. No tissue available for histological analysis.	

		Expert #2 As involves laser, needs to be performed by competent or well-supervised staff to minimise laser-associated risks to patient and staff (very rare).	
		Expert #3 There is an uncertainty regarding the durability of the outcome after green light laser prostatectomy and also whether it adds value compared to the bipolar TURP, which cases less bleeding that the traditional monopolar TURP and does not have risk of TURP syndrome.	
		Expert #4 NA	
		Expert #5 NA	
		Expert #6 n/a	
		Expert #7 Uncertainties regarding its efficiency for prostates over 150g (very big).	
		Expert #8 No concerns if surgeons are well trained	
		Expert #9 N/A	

		Expert #10 Potentially high rates of patients needing re-do surgery in future	
		Expert #11 1. Long term follow up data	
17	Is there controversy, or important uncertainty, about any aspect of the procedure/technology?	Expert #1 As above regarding tissue diagnosis.	
		Expert #2 Not that I am aware of.	
		Expert #3 As above	
		Expert #4 NA	
		Expert #5 NA	
		Expert #6 n/a	
		Expert #7 -	
		Expert #8 No	

		Expert #9 N/A	
		Expert #10 Potentially high rates of patients needing re-do surgery in future	
		Expert #11 Not that I am aware of	
18	If it is safe and efficacious, in your opinion, will this procedure be carried out in (please choose one):	Expert #1 Most or all district general hospitals.	
		Expert #2 Most or all district general hospitals.	
		Expert #3 Cannot predict at present.	
		Expert #4 Cannot predict at present.	
		Expert #5 Most if not all NHS hospitals.	
		Expert #6 Most or all district general hospitals. BUT BPH care should be concentrated in regional hubs for best outcomes and efficiency	
		Expert #7	

		Most or all district general hospitals.	
		Expert #8 Most or all district general hospitals.	
		Expert #9 Most or all district general hospitals.	
		Expert #10 Most or all district general hospitals.	
		Expert #11 Most or all district general hospitals.	
19	Please list any abstracts or conference proceedings that you are aware of that have been recently presented / published on this procedure/technology (this can include your own work). Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.	Expert #1 http://dx.doi.org/10.1136/bmjopen-2018-028855	
		Expert #2 Haudebert C. PT322 Diabeted may compromise the functional outcomes of Greenlight laser XPS-180W photoselective vaporization of the prostate. European Association of Urology Congress July 2020. Chavarriaga Soto J. P0083 Outpatient 180 W XPS GreenLight Laser photoselective vapolization of the prostate: Seven year experience. European Association of Urology Congress 2021 Reale GFM. PT316 Surgical performance of greenlight laser therapy for benign prostatic	

		hyperplasia: preliminary results in terms of operative profile, safety and functional outcomes from a retrospective multicentre Italian database study. European Association of Urology Congress July 2020. Ghobrial FK. P0088 Greenlight (532nm) laser transurethral prostatectomy for treatment of benign prostate obstruction using XPS-180Watt system, does it pass the test of time? European Association of Urology Congress 2021 Ibrahim A. P0086 GreenLight Laser prostatectomy: are outcomes sustainable after a decade of surgery? A single center experience with up to 15 years' followup. European Association of Urology Congress 2021	
		Expert #3 I think NICE should be aware of BAUS BOO audit, the results of which have been presented at BAUS 2021 and are about to be published formally.	
		Expert #4 NA	
		Expert #5 I selected some landmark reviews (meta-analysis / GOLIATH randomised study) 1. Lai S, Peng P, Diao T, Hou H, Wang X, Zhang W, Liu M, Zhang Y, Seery S, Wang J. Comparison of photoselective	

		green light laser vaporisation versus traditional transurethral resection for benign prostate hyperplasia: an updated systematic review and meta-analysis of randomised controlled trials and prospective studies. BMJ Open. 2019 Aug 21;9(8):e028855. doi: 10.1136/bmjopen-2018-028855. PMID: 31439603; PMCID: PMC6707662. 2. Thomas JA, Tubaro A, Barber N, d'Ancona F, Muir G, Witzsch U, Grimm MO, Benejam J, Stolzenburg JU, Riddick A, Pahernik S, Roelink H, Ameye F, Saussine C, Bruyère F, Loidl W, Larner T, Gogoi NK, Hindley R, Muschter R, Thorpe A, Shrotri N, Graham S, Hamann M, Miller K, Schostak M, Capitán C, Knispel H, Bachmann A. A Multicenter Randomized Noninferiority Trial Comparing GreenLight-XPS Laser Vaporization of the Prostate and Transurethral Resection of the Prostate for the Treatment of Benign Prostatic Obstruction: Two-yr Outcomes of the GOLIATH Study. Eur Urol. 2016 Jan;69(1):94-102. doi: 10.1016/j.eururo.2015.07.054. Epub 2015 Aug 15. PMID: 26283011. 3. Elshal AM, Elkoushy MA, El-Nahas AR, Shoma AM, Nabeeh A, Carrier S, Elhilali MM. GreenLight™ laser (XPS) photoselective vapo-enucleation versus holmium laser enucleation of the prostate for the treatment of symptomatic benign prostatic hyperplasia: a randomized controlled study. J Urol. 2015 Mar;193(3):927-34. doi:	

		10.1016/j.juro.2014.09.097. Epub 2014 Sep 28. PMID: 25261801. 4. Corbel L, Della Negra E, Berquet G, Codet YP, Boulière F, Braguet R, Trifard F. Vaporisation laser prostatique par GreenLight (180 W) en ambulatoire: évaluation prospective sur 115 patients [Ambulatory prostate photoselective vaporisation with GreenLight laser (180W): prospective evaluation from 115 patients]. Prog Urol. 2014 Oct;24(12):733-7. French. doi: 10.1016/j.purol.2014.08.238. Epub 2014 Sep 17. PMID: 25241244.	
		Expert #6 Hundreds of papers	
		Expert #7 Recent work – Trail, M., Good, D., Clyde, D., Brodie, K., Leung, S., Simpson, H., Kata, S. G., Tsafrakidis, P., Chapman, R. A., Mitchell, I., Janjua, K., & Al Jaafari, F. (2021). Day Case GreenLight Laser Photoselective Vaporisation of the Prostate (GL-PVP): Evaluation of Outcomes from a District General Hospital Experience of 538 Cases. *Journal of Endoluminal Endourology*, *4*(3), e8-e16. https://doi.org/10.22374/jeleu.v4i3.128 Abolazm AE, El-Hefnawy AS, Laymon M, Shehab-El-Din AB, Elshal AM. Ejaculatory Hood Sparing versus Standard Laser Photoselective Vaporization of the Prostate: Sexual and Urodynamic Assessment through a Double	

		Blinded, Randomized Trial. J Urol. 2020 Apr;203(4):792-801. doi: 10.1097/JU.0000000000000685. Epub 2019 Nov 25. PMID: 31763948. Campobasso D, Ferrari G, Frattini A. Greenlight laser: a laser for every prostate and every urologist. World J Urol. 2020 Oct 26. doi: 10.1007/s00345-020-03499-z. Epub ahead of print. PMID: 33104906. Stone BV, Chughtai B, Kaplan SA, Te AE, Lee RK. GreenLight laser for prostates over 100ml: what is the evidence? Curr Opin Urol. 2016 Jan;26(1):28-34. doi: 10.1097/MOU.0000000000000237. PMID: 26626882.	
		Expert #8 I have presented > 10 abstracts myself at various meetings internationally. Read the publications from Goliath	
		Expert #9 Comparative Study Arch Ital Urol Androl 2020 Oct 1;92(3). doi: 10.4081/aiua.2020.3.169. Comparison of GreenLight 180-W XPS laser vaporization versus transurethral resection of the prostate: Outcomes of a single regional center Daniele Mattevi 1 , Lorenzo Luciani, Rosa Spina, Claudio Divan, Stefania Cicuto,	

		Tommaso Cai, Valentino Vattovani, Marco Puglisi, Stefano Chiodini, Gianni Malossini A European multicenter randomized noninferiority trial comparing 180 W GreenLight XPS laser vaporization and transurethral resection of the prostate for the treatment of benign prostatic obstruction: 12-month results of the GOLIATH study. J Urol. 2015 Feb;193(2):570-8. doi: 10.1016/j.juro.2014.09.001. Epub 2014 Sep 16. PMID: 25219699 Clinical Trial. Bachmann A, Tubaro A, Barber N, d'Ancona F, Muir G, Witzsch U, Grimm MO, Benejam J, Stolzenburg JU, Riddick A, Pahernik S, Roelink H, Ameye F, Saussine C, Bruyère F, Loidl W, Larner T, Gogoi NK, Hindley R, Muschter R, Thorpe A, Shrotri N, Graham S, Hamann M, Miller K, Schostak M, Capitán C, Knispel H, Thomas JA.	
		Expert #10 N/A	
		Expert #11 I am not aware of any recent abstract or conference proceedings	
20	Are there any major trials or registries of this procedure/technology currently in progress? If so, please list.	Expert #1 Not to my current knowledge	
		Expert #2	

		Not that I am aware of	
		Expert #3 Not aware	
		Expert #4 ?	
		Expert #5 NA	
		Expert #6 No	
		Expert #7 n/a	
		Expert #8 Goliath study	
		Expert #9 Not that I am aware of – other than a study in France looking at the safety of the procedure in patients with a bleeding tendency.	
		Expert #10 N/A	
		Expert #11 I am in the process of setting up a region wide registry (Yorkshire & Humber)	

		Depending on how this evolves, I am in talks with users in other regions for collaboration on a nation-wide registry for all Greenlight users	
21	Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?	Expert #1 20% of target population	
		Expert #2 According to the BAUS national audit, approximately 1620 BPH procedures were performed in a year. I estimate ~80% of those would be eligible for this technology.	
		Expert #3 I think about a half of the target population of men with BPH seeking surgical treatment would be suitable for the technology.	
		Expert #4 Currently approx. 25,000 patient per year are suitable but only a minority of these patients will end up having this technology through a mixture of restricted availability and newer less invasive options	
		Expert #5 Between 40-50 % of target population.	
		Expert #6 20k/year	
		Expert #7	

		I would suspect that at least 60-70% of patients with bladder outflow obstruction would be eligible for thus procedure.	
		Expert #8 UK 10,000	
		Expert #9 25-40% - approx. 4000-5000	
		Expert #10 Potentially 70-75% of target population.	
		Expert #11 In my opinion- most patients who need a TURP would be eligible for this procedure Around 25,000 bladder outflow surgeries are carried out annually in the UK. Based on the BAUS National Snapshot Audit data, currently GLL is offered to around 10% of all patients. This might increase with the GIRFT recommendations. So around 2500-3000 procedures based on the current available data.	

22	Are there any issues with the usability or practical aspects of the procedure/technology?	Expert#1 Cost, training	
		Expert#2 None, beyond comments mentioned previously.	
		Expert#3	

		The surgeon requires training with a proctor to perform the procedure safely and effectively. It is not routinely provided in the registrar training programmes to my knowledge, whereas TURP is one of the indicative training procedures.	
		Expert #4 NA	
		Expert #5 NA	
		Expert #6 no	
		Expert #7 no	
		Expert #8 No	
		Expert #9 No	
		Expert #10 Teaching and training – but plenty of mentors available in UK. Availability of laser machine is biggest hurdle due to cost, in current pandemic situation.	
		Expert #11 1. Capital costs (purchase or hire) & individual laser fibre costs	

		2. Initial training costs (short learning curve compared to other procedures) 3. Theatre time: takes between 10-20% longer time over TURP	
23	Are you aware of any issues which would prevent (or have prevented) this procedure/technology being adopted in your organisation or across the wider NHS?	Expert#1 Cost, training, no tissue diagnosis	
		Expert#2 No	
		Expert#3 Training of the surgeon and the staff, as well as availability of the technology, although I am aware that the laser is placed on pay per fibre basis by the company.	
		Expert #4 Less invasive technologies e.g. Rezum and Urolift which can be administered and performed in an out patient setting under LA	
		Expert #5 NA	
		Expert #6 Poor previous training and standardisation	
		Expert #7 no	
		Expert #8 No	

		Expert #9 No	
		Expert #10 Perceived lack of efficacy long term and cost of initial purchase.	
		Expert #11 1. The negative experience from the 80W Greenlight laser is likely to have affected the opinion of clinicians- the 80w laser was marketed heavily, with little training and mentorship. Also the volume clearance was sub-optimal, leading to higher rate of secondary interventions. The immediate post-operative period was also associated with dysuria and prostatitis. The above issues have been addressed by device development and subsequent evidence showing that the side effect profile has improved 2. Costs of adopting the new technology	
24	Is there any research that you feel would be needed to address uncertainties in the evidence base?	Expert#1 No	
		Expert#2 None specific to this technology	
		Expert#3	

		Randomised comparison to bipolar TURP and other technologies (HOLEP, PAE, Rezum and Urolift)	
		Expert #4 NA	
		Expert #5 NA	
		Expert #6 Impossible to run RCT's of high risk patients as standard of care (TURP) may be unethical	
		Expert #7 Further research for the efficacy of the procedure for the very large glands.	
		Expert #8 No	
		Expert #9 Perhaps a study looking at bleeding risk with this approach – data should be available soon see below: Stop or Ongoing Oral Anticoagulation in Patients Undergoing PVP (SOAP) (SOAP) – underway in France study commenced 2017. V Misrai et al	
		Expert #10 Comparison trials vs other daycase surgery treatments for BPH – e.g.: Rezum and Urolift.	

		Understanding benefit of this current treatment in high risk (anticoagulated) patients.	
		Expert #11 1. Long term data on outcomes is lacking 2. Data in the NHS settings on outcomes in high risk groups like urinary retention	
25	Please suggest potential audit criteria for this procedure/technology. If known, please describe: − Beneficial outcome measures. These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured. − Adverse outcome measures. These should include early and late complications. Please state the post procedure timescales over which these should be measured	Expert#1 Beneficial outcome measures: Assess symptom improvement with IPSS and uroflowmetry Assess reintervention rate Assess complication rate Adverse outcome measures: Continence Failure to improve symptoms Reintervention rate less than 10 years	
		Expert#2 See point 15 above.	
		Expert#3 Beneficial outcome measures: - Flow rate, IPSS and quality of life after 3 months and 5 years - Hospital stay	

		Adverse outcome measures: - Rate and type of postoperative complications over 5 years - Secondary procedures over 5 years Early complications include - Bleeding - Postoperative retention - Infection and urosepsis - dysuria Late complications include - stricture - prostatic regrowth - erectile dysfunction - incontinence - retrograde ejaculation	
		Expert #4 Beneficial outcome measures: IPSS Length of stay Adverse outcome measures: Complications Reoperation rate Transfusion rates	

		Expert #5 Beneficial outcome measures: PROMS/Successful TWOC / Flow Test/ Bladder scan/Hospital stay Adverse outcome measures: Bleeding / re-hospitalisation/ persistent symptoms/ failed treatment / general complications (DVT/PE/Infection/sepsis)/Incontinence	
		Expert #6 Beneficial outcome measures: Adverse outcome measures:	
		Expert #7 Beneficial outcome measures: Age, ASA score, comorbidities, prostate volume, IPSS, post void residual, flow rate, QoL score, IIEF-2 score, ejaculation (yes/no). Successful Trial without catheter. Days of hospitalisation (True day case vs 23hr stay vs inpatient). Ideally all patients should be reviewed at 3-4 months post op with identical comparators (pre- vs post op) Adverse outcome measures	

		Retreatment rates in the first year. Strictures rate in the first 1 year. Failed Trial without catheter post treatment. Bleeding requiring transfusion during the same admission). Readmission within 1 month.	
		Expert #8 Beneficial outcome measures: Adverse outcome measures:	
		Expert #9 Beneficial outcome measures: PROM's at 3-6 months for early outcome and then 2 years for audit Satisfaction scores – would they recommend yes or no etc Adverse outcome measures: TWOC rates / 30 day readmission rates / retreatment rates in the first 1-2 years	
		Expert #10 Beneficial outcome measures: IPSS, SHIM scores and QOL scores during follow up (according to clinical protocols). Adverse outcome measures:	

		Need for re-intervention with same or different treatment modality for BPH.	
		Expert #11 Beneficial outcome measures: Audit should cover long term data (>36 months) 1. IPSS and Qmax improvements 2. Day case rates 3. Successful TWOC rates (along with timing of TWOC) in patient with urinary retention 4. Re-operation / Secondary intervention rates 5. Outcomes in patients on anticoagulants/ anti-platelets agents and the elderly Adverse outcome measures: 1. Infection and sepsis rates (Early complication- up to 12 months) 2. Erectile dysfunction (Early complication- up to 12 months) 3. Storage LUTS (Early complication –up to 12 months) 4. Re-operation/ Secondary intervention rates (long term >36 months)	
26	Please add any further comments on your particular experiences or knowledge of the procedure/technology	Expert#1 n/a	
		Expert# 2 Generally, from colleagues that have been regularly using this technology, there has been good experience in terms of its safety and	

		efficacy. In my specialist practice of BPH, I have encountered patients that have previously had Greenlight laser PVP and require further BPH surgery because of prostatic regrowth after several years. However, reintervention is a known fact for clinicians and well-counselled patients, although this is overcome by enucleated techniques such as HoLEP which have an exceptionally low reintervention rate.	
		Expert#3 n/a	
		Expert #4 NA	
		Expert #5 n/a	
		Expert #6 n/a	
		Expert #7 In my experience I believe that Greenlight laser is a safe operation and can be offered to high risk patients given its safety profile in comparison to TURP. Most frail patients can be optimised by the anaesthetic/medical teams to allow for their operation to take place. This operation will be particularly useful in the COVID recovery era given the convincing long term outcomes.	
		Expert #8	

		I regard myself as an expert in the procedure.	
		Expert #9 It is a very reliable procedure. Bleeding is seldom a problem.	
		Expert #10 n/a	
		Expert #11 My experience 1. As a Senior Clinical Fellow at Stepping Hill Hospital, I have used the 80w Greenlight Laser (after appropriate training and mentoring in the unit) and independently performed close to 50 procedures 2. As Consultant Urologist at Sheffield Teaching Hospital- I underwent training and mentorship for the 180w Greenlight laser in 2018. I set up the laser service along with my colleague Mr Patrick Cutinha and to date have performed >250 procedures 3. I run the BPH training course- dry and wet lab (cadaveric) for the urology trainees in Yorkshire and Humber 4. I have been recognised as a trainer and proctor by the manufacturer (Boston Scientific) and involved in proctorship of Consultant colleagues in the UK since Sep 2021.	

Appendix 7

Is vapo-resection (also referred to as vapo-incision) the same as or comparable to PVP and HoLEP? Is this a commonly used procedure?

Expert #1	Gordon Muir
Expert #2	Feras Al Jaafari
Expert #3	Marios Hadjipavlou
Expert #4	Andrew Thomas
Expert #5	Iqbal Shergill
Expert #6	Richard Hindley
Expert #7	Ian Pearce
Expert #8	Maya Harris

Collated responses

Expert #1	It's a modification of GreenLight vaporisation which cuts chips out. Very few people use it. Results the same as GreenLight but anecdotally slightly higher bleeding. Very little data except single centre series.
Expert #2	Vapo-resection/incision is not a technique that we use routinely. In the past this was attempted with Holmium/Thulium but was not successful and indeed inferior to PVP. On the other hand Vapo-enucleation is a different technique and is used in combination with anatomical PVP (allows to debulk a large amount of the prostate). There is a good RCT published in the Americal Journal of Urology comparing it to HoLEP, please see below. Elshal AM, Elkoushy MA, El-Nahas AR, Shoma AM, Nabeeh A, Carrier S, Elhilali MM. GreenLight™ laser (XPS) photoselective vapo-enucleation versus holmium laser enucleation of the prostate for the treatment of symptomatic benign prostatic hyperplasia: a randomized controlled study. J Urol. 2015 Mar;193(3):927-34. doi: 10.1016/j.juro.2014.09.097. Epub 2014 Sep 28. PMID: 25261801.
Expert #3	I understand that vaporesection is a combination if vapourisation and resection using Greenlight technology - it is certainly different from HoLEP or any enucleating technique, but probably relatively similar to PVP.
Expert #4	Vaporesection is a term where the laser is used to simultaneously vaporise prostate tissue and creates chips of tissue to remove - enucleation - akin to holep.
Expert #5	Vapo-resection or vapo-incision would not really be same as PVP and HOLEP really. More akin to TURP really, but usually refers to Thulium laser typically. NOT commonly used in UK.

Expert #6	Hi My short answer is that I think vapo-resection tends to used when referring to the thulium laser which is a laser used very infrequently to treat BPH in the UK. BW, Richard PS If you need another opinion [redacted] would be good as he is very knowledgeable with regards to thulium.
Expert #7	Vapo-resection is PVP and essentially vaporises the prostate using a different type of laser to HoLEP.
Expert #8	Vapororesection and incision are different to the standard procedure and should not be in the review.

Appendix 8

Additional questions sent to clinical experts and Company 14/01/2022

1. Within the original economic model, the proportion of patients undergoing day-case surgery (no overnight stay) was modelled as 35.96% in patients receiving GreenLight, 35.96% in HoLEP and 4.08% in TURP. The EAC has updated the day-case proportion for GreenLight (68% from the study by Trail et al. 2021), which also broadly corresponds to a mid-point of the estimates shared by clinical experts in response to earlier questions. However can you confirm that the proportion of day-cases is still appropriate for HoLEP (35.96%) and TURP (4.08%) when conducted in a UK NHS setting?

2. The GreenLight XPS Instructions for Use state that everyone in the room is required to wear protective eyewear. Can you advise the **total** number of people (including all staff and the patient) that will be in the room when a GreenLight procedure for BPH is conducted?

3. Can you confirm the number of people (including all staff and the patient) that would be in the room when a HoLEP procedure for BPH is conducted?

Expert #1	Feras Al Jaafari
Expert #2	Andrew Thomas
Expert #3	Gordon Muir
Expert #4	Richard Hindley
Expert #5	[redacted]
Expert #6	Marios Hadjipavlou
Expert #7	Sanjay Rapal
Expert #8	Amr Emara
Expert #9	Aniruddha Chakravarti
Expert #10	Maya Harris

Collated responses

Expert #1	1. The answer depends of your definition of day case - if it is true daycase (i.e. patients sleeps in their bed that night at home) then yes, I agree these are realistic figures. 2. and 3. The theatre staff is as follows on a typical GLL/HoLEP list: a. 1 surgeon b. 1 anaesthetist c. 1 ODP d. 2 nurses on the floor (runners - on flooring duties)

	e. 1 nurse on laser safety duty f. 1 scrub nurse In addition, there might be a trainee surgeon, and anaesthetic assistant and/or anaesthetic trainee. In average 7-10 people in theatre - all requiring laser goggle (Holmium goggles for HoLEP and Greenlight goggles for GLL)
Expert #2	For laser cases - numbers in room do vary between hospitals . From a minimum 4 staff , 5 usually . Also patient in theory should wear protective glasses. 6 in total Your day case rates I think are about right for all 3 procedures.
Expert #3	1. We manage 90% Day case at King's for Greenlight without selection. The others are fair but few units are achiving them 2. Usually 6 if only one surgeon. The laser glasses don't cause any restriction 3. Again, 6 or 7
Expert #4	Happy to try and help. The historic economic model would I suspect be based on HES data and/or published data. It is a statement of fact that we need to be encouraging centres to provide daycase procedures in order to reduce the burden on the NHS waiting list and allow men to receive their treatment with less of a wait time. I think the new figures for Greenlight and HoLEP are reasonable but certainly at the upper end of what is achievable. For TURP I suspect nationwide only 4% go home the same day but there are centres achieving very high rates of same day discharge for bipolar TURP (Portsmouth for example [redacted] Perhaps we need a figure therefore which is higher than 4% - for example if we were aspirational and aimed for 20% this would have a huge impact across many sites. However, Trusts may do better to look at other technologies such as GL and HoLEP over TURP if they wish to achieve high rates of same day discharge. If you would like I can copy in [redacted] for his insight (as a HoLEP expert). TURP will not achieve the same day case rates as greenlight for example but 4% feels like it is rather on the low side. However, I guess for your calculations you need real world UK practice upon which to arrive at something meaningful? Model Hospital may be useful to extract the latest proportions possibly. Regarding eyewear – it will be the same for HoLEP and GL. The patient, the anaesthetist, the surgeon, a laser operator, a

	scrub nurse and perhaps an ODP. My estimate would be 5-6 max in theatre.
Expert #5	[redacted]

	[redacted] [redacted])
Expert #6	1. I don't think an assumption can be made on the proportion of the remaining cases - with time, more and more surgeons start performing HoLEP and they sometimes switch their practice to perform this as day case as they build their experience and confidence. There are too many variables to account for. 2. There would typically be a minimum of 6-7 people (patient, anaesthetist, ODP, surgeon, scrub nurse, 1-2 supporting staff). Often there may be medical students or more junior doctors, or an anaesthetic trainee, or a company rep, etc, therefore the number may be up to 10-12. A minimum of 12 sets of glasses are usually needed for a well equipped theatre (departments need to account for breakages, glasses going missing, etc). 3. For HoLEP I would estimate the same as above.
Expert #7	1. Day case rates for HOLEP in UK: a published case series from Archer et al 2018 reported 35.3%-day case rates. I suspect across the UK; the range would be somewhere between 35% and 60%. For TURP, there is no published data which I am aware of; anecdotally I feel the range would be 4-10. 2. The number of people in the theatre will depend on the composition of the theatre team which might vary slightly from centre to centre- a minimum of 7 will be in the room (patient, anaesthetist, ODP, scrub nurse

	x1, circulating nurse x1, health care support worker x1, Surgeon x1). 3. I don't have experience of doing HOLEP but have observed other colleagues doing this procedure- they will have similar numbers in theatres as outlined in response 2.
Expert #8	1. Yes. 2. Minimum of 7 (patient - surgeon – anaesthetist – OPD – Circulating nurse – scrub nurse – laser operator), additional trainee can be present. 3. Same 7.
Expert #9	1. I do not think 68% of an unselected population undergoing Green light laser PVP can be discharged on the same day universally across all NHS hospitals unless they are chosen carefully (fit patients with no significant comorbidity, small-medium size prostates, uncomplicated procedure, and adequate home support) and a pre organised pathway exists. The number for HoLEPs that can be discharged on the same day will also depend on case selection (fit patients with no significant comorbidity, mobile, with adequate home support etc), and in my estimate it will be around 20% across the whole NHS without a pre-set pathway. The percentage of patients undergoing TURP that can be sent home same day has been much greater than 4%, also depending on case selection and support available at home. 2. The number of people in theatre during a Green Light procedure is like what it will be for HoLEP or TURP which is around 8-9.
Expert #10	1. Thanks, I do not think there are any TURP day cases and I am unable to comment on HOLEP, as our centre does not perform it. 2. There is usually the following people – anaesthetist, an anaesthetic nurse, the patient, laser operator, scrub nurse, a runner nurse (6) and maybe one or two trainees. 3. Unable to comment as I do not perform HOLEP.

Appendix 9

GID-MT564 GreenLight XPS

Meeting with David Rawlings, Clinical Scientist, Laser Protection Adviser, NuTH

Friday 14 January 2022

Microsoft Teams

In Attendance: David Rawlings (DR), Kim Keltie (KK), Emma Belilios (EB), Rachel O'Leary (RO)

1. Purpose of the meeting:

Newcastle External Assessment Centre (EAC), supporting the NICE Medical Technologies Evaluation Programme (MTEP) have been commissioned to update the assessment report on GreenLight XPS for treating benign prostatic hyperplasia. The EAC have some questions about the safety requirements for GreenLight laser procedures compared with holmium laser enucleation of the prostate (HoLEP).

2. Questions

i. What are the safety requirements for GreenLight laser procedures?

Response:

KTP lasers are well established. Protective goggles specifically for GreenLight wavelengths (532mn) are required. It is important that the goggles are clear; tinting can impair vision. DR has found suitable 532mn specified goggles available that are glass, with about 75% clarity. Different goggles are required for HoLEP. However no large difference in cost of protective eyewear required between the two procedures.

Goggles are an encumbrance. If GreenLight service provision is being set up from scratch, regular users should have the opportunity to have their own goggles and to have a choice in the type of goggles. Suppliers will send out sample frames to try best fitting.

GreenLight procedure must be done in a laser safe/laser controlled area with clear signage at each entrance. Some rooms have doors that automatically lock when the laser is on (although this is not an essential requirement). The same requirements are needed for HoLEP. This may be a consideration for hospitals introducing GreenLight as a day-case procedure (as it will need to be conducted in a laser controlled theatre).

A clear advantage of the GreenLight laser is that you can definitely see the green laser which you may not be able to do with HoLEP (unless there is an aiming or guide beam).

GreenLight laser is applied through a fibre - the fibres are specific to the device. Single use fibres are preferable. Danger to the operator is not just light emitted at the end of the fibre (controllable), but also, if the fibre breaks (due to a fault, or poor technique).

ii. Is the cost of googles for GreenLight procedures comparable with the cost of goggles for other laser procedures?

Response:

Yes. Cost will depend on frames they choose, but not wildly different. Cleaning requirements will also be the same.

iii. What is the lifespan of laser safety goggles?

Response:

Around five years (though user should check every time they wear them for any damage). Laser Physics UK (supplier) can give comparative costs.

iv. The EAC has searched FDA MAUDE Database which reports some fibre breakage. Is this likely to be an issue for GreenLight?

Response:

GreenLight uses a multi-core fibre with many optical modes in it. If it breaks, light will scatter. The fibre is within a sheath, so in case of breakage, the light will interact with the sheath and start to burn it (the light doesn't reach the patient through the sheath, so no patient harm). DR was aware of a recent incident when multiple fibres broke (due to poor technique) and the surgeon burnt his thumb. This is no different to holium laser.

v. Do patients need to wear protective eyewear during BPH surgery?

Response:

Current guidelines state that while this is essential for patients receiving treatment to the head and neck area it is optional otherwise. Whilst it is not essential for prostate surgery, it will be subject to local risk assessment.

NICE National Institute for Health and Care Excellence

National Institute for Health and Care Excellence

Centre for Health Technology Evaluation

Pro-forma Response

External Assessment Centre Report factual check

GreenLight XPS for treating benign prostatic hyperplasia

Guidance Update Assessment Report

Please find enclosed the assessment report prepared for this assessment by the External Assessment Centre (EAC).

You are asked to check the assessment report from Nuth to ensure there are no factual inaccuracies contained within it. If you do identify any factual inaccuracies you must inform NICE by 9am, **28th April 2022** using the below proforma comments table. All your comments on factual inaccuracies will receive a response from the EAC and when appropriate, will be amended in the EAC report. This table, including EAC responses will be presented to the Medical Technologies Advisory Committee and will subsequently be published on the NICE website with the Assessment report.

28th April 2022

NICE National Institute for Health and Care Excellence

Issue 1

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 11 *"A Markov model approach that modelled longer-term consequences over a 5-year time horizon showed GreenLight to be cost-saving by £305 and £270 when compared with TURP and HoLEP respectively."*	Please remove this result and report a different base-case from the Markov model that does not use the mean length of stay for GreenLight and HoLEP of 1.6 days. We suggest using 0.7 applied in the MTG49 model, sourced from Ajib et al. 2018 and accepted by the EAC as part of the MTG49 review. Alternatively, report both results and state the limitations of using data from the OPCS codes and assuming the same length of stay for both GreenLight and HoLEP which is clinically unlikely. Suggested text below: *"A Markov model approach, using a prior model reviewed under NICE MTG49 for a different technology, modelled longer-term consequences over a 4-year time horizon. After minor adjustments made by the EAC, including updating the cost of GreenLight, this model showed GreenLight to be cost-saving by £630.70 and £712.30 when compared with TURP and HoLEP respectively in an average risk population.* *The EAC further updated this model, extending the time horizon to 5 years and adjusting the length of stay from 0.7 to 1.6 for GreenLight and from 2 to 1.6 for HoLEP. This showed*	The original model reviewed by NICE and published under MTG49 reported higher cost savings with GreenLight compared to TURP and HoLEP. It is therefore confusing to report very different results from the same model without making it clear to the reader the key changes that were made by the EAC. This is particularly important given there is uncertainty around the length of stay for GreenLight and the limitations to the source selected by the EAC that reports the combined length of stay for GreenLight and HoLEP. We contend that the length of stay for GreenLight of 0.7 applied in MTG49 model, sourced from Ajib et al. 2018 and accepted by the EAC as part of MTG49 review, is a more robust source because it does not combine data for GreenLight and HoLEP. Ajib et al. 2018 was an analysis of 5 year prospectively	Thank you for your comment. This is the Company's view on the EAC choice of base case parameters, and is not a factual inaccuracy. No change required.

	GreenLight to be cost-saving by £305 and £270 when compared with TURP and HoLEP respectively. This scenario is expected to underestimate the cost-saving with GreenLight by assuming the same length of stay for GreenLight and HoLEP. A substantially higher proportion of GreenLight procedures are expected to be performed as day-case, relative to HoLEP. Four clinical experts agreed with 68% of GreenLight cases being performed as day-case compared to 36% of HoLEP procedures. The mean length of stay for GreenLight is therefore reasonably expected to be considerably lower than HoLEP and close to 1."	gathered data on GreenLight XPS-180 procedures. The clinical experts consulted during this process accepted the estimates that 68% of GreenLight procedures are performed as day-case compared to 36% of HoLEP. It is therefore contradictory to assume the mean length of stay for both technologies would be the same.	

Issue 2

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pages 15-16 *"During anatomical PVP once the capsule at the apex of the prostate is identified, a bilateral incision is created lateral to the verumontanum and the tip of the rectoscope is used to find the anatomical plane between the prostatic capsule and the adenoma."*	'Rectoscope' should be amended to 'resectoscope' to read: *"During anatomical PVP once the capsule at the apex of the prostate is identified, a bilateral incision is created lateral to the verumontanum and the tip of the resectoscope is used to find the anatomical plane between the prostatic capsule and the adenoma."*	Correction of terminology	Thank you for your comment. This has been changed in the report.

Issue 3

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 17 *"Greenlight XPS PVP is performed under a general anaesthetic and may be done as either a day-case or an inpatient procedure."*	We propose a slight amendment to this statement: *"Greenlight XPS PVP is generally performed under a general anaesthetic, although can also be performed under spinal anaesthetic, and may be done as either a day-case or an inpatient procedure."*	Slight amendment of this statement to align with current clinical practice.	Thank you for your comment. The EAC has amended the text to the following: "Greenlight XPS PVP is generally performed under a general anaesthetic, can also be performed under spinal anaesthetic, and may be done as either a day-case or an inpatient procedure."

Issue 4

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pages 18-19 *"The European Association of Urology (EAU) Guideline for the Management of Non-neurogenic Male LUTS 2021 reports that GreenLight 180 W PVP "seems to be safe for the treatment of patients receiving antiplatelet or anticoagulant therapy"; however, the level of available evidence was reported as "low"."*	*We propose that this should be updated to reflect most recent guidelines as follows:* *"The European Association of Urology (EAU) Guideline for the Management of Non-neurogenic Male LUTS 2021 and 2022 report that GreenLight 180 W PVP "seems to be safe for the treatment of patients receiving antiplatelet or anticoagulant therapy"; however, the level of available evidence was reported as "low"."*	The European Association of Urology (EAU) Guideline for the Management of Non-neurogenic Male LUTS 2022 has been published and also reports this guideline for GreenLight 180 W PVP.	Thank you for highlighting this. The EAU Guideline for the Management of non-neurogenic male LUTS update was published in March 2022, which was after the completion of the EAC review of clinical evidence. We have amended the report to state the latest guideline and changed the hyperlink to the 2022 report only.

Issue 5

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 23 *"The Company identified a total of 65 studies they considered were relevant and within the scope of the decision problem. The EAC excluded 40 of these, Table 2."*	Table 2 is missing on page 23 of the report.	Table 2 is missing on page 23 of the report. After notifying the NICE team of this discrepancy, they informed us that Table 2 had been moved to the appendices section (Appendix A4) on page 185.	Thank you for your comment. The table of exclusion was moved to Appendix B4, the hyperlink has now been updated. Table numbers have been updated accordingly.

Issue 6

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 100 *"The Newcastle EAC notes that currently available procedure (OPCS) codes combine procedures together, however from NHS activity reports from 2019/20, the mean length of stay for TURP (based on 11,420 admissions with primary procedure code M65.3 Endoscopic resection of prostate not elsewhere classified, which combines mono- and bi-polar TURP) is 2.3 days, and 1.6 days for GreenLight or HoLEP (based*	We propose to either remove these sentences and replace all scenarios reporting results using a length of stay for Greenlight of 1.6 with a more robust source, or to add the following sentence to this paragraph and a similar note when these scenarios are reported thereafter: *"This approach to estimating length of stay is likely to overestimate the mean length of stay for GreenLight and underestimate the length of stay for HoLEP because a substantially higher proportion of GreenLight procedures are expected to be performed as day-case, relative to HoLEP. Four clinical experts agreed with 68% of GreenLight cases being performed as*	Using this source and applying a length of stay of 1.6 for GreenLight is not appropriate, for the reasons outlined in Issue 1. We contend that this length of stay should only be reported in one scenario analysis and should not be applied in multiple scenarios or reported in the executive summary. Where this length of stay is applied, the limitations of this source should be clearly acknowledged.	Thank you for your comment. This is the Company's view on the EAC choice of base case parameters, and is not a factual inaccuracy. No change required. A length of stay of 0.7 days was applied to the GreenLight arm in the Rezum model, which was derived from a non-comparative single centre study conducted in Canada of 370 men recruited between 2011 and 2016 treated by a single surgeon (Ajib *et al.* 2018). The length of stay applied by the EAC was derived from all NHS activity of 11,420 admissions in 2019/20; and the EAC has listed limitations of using this

on 3,943 admissions with primary procedure code M65.4 Endoscopic resection of prostate using laser, which combines GreenLight and HoLEP).” Page 142 *“As noted in Section 9.2, the EAC consider the length of stay of 1.6 days for GreenLight or HoLEP and 2.3 days for TURP to be more appropriate based on OPCS codes from NHS activity from 2019/20”* Pages 137-140, Table 26 All scenarios reporting a length of stay of 1.6	*day-case compared to 36% of HoLEP procedures. The mean length of stay for GreenLight is therefore reasonably expected to be considerably lower than HoLEP.”*		source (the inability to differentiate GreenLight from HoLEP procedures). The EAC notes that there is a lack of robust published evidence comparing length of stay between GreenLight and HoLEP. The only new evidence identified by the EAC which included both GreenLight and HoLEP (this arm also included ThuLEP and did not report outcomes exclusively) was the non-randomised study by Mathieu *et al.* (2017), which reported the following mean (SD) length of stay: - GreenLight PVP (n=51): 2.8 (2.9) days - HoLEP/ThuLEP (n=64): 2.6 (2.5) days Seven Clinical experts have stated that 1.6 days for GreenLight and HoLEP and 2.3 days for TURP was appropriate. One explicitly stated that length of stay was shorter for GreenLight than HoLEP, and one explicitly stated that length of stay was shorter for bipolar than monopolar TURP (EAC Correspondence Log, 2022). The EAC also notes of the 11 studies reporting length of stay (see Table 11 in the EAC Assessment Report) that only 1 reported a median length of stay for GreenLight of less than 1 day (Meskawi *et al.* 2019).

			Modelling uncertainty in length of stay was included by the EAC in threshold analysis (see page 144): *"To account for the large uncertainty the EAC conducted additional univariate threshold analysis, and found that if the procedure duration of TURP and HoLEP reduced below 43.7 and 60.0 minutes respectively (relative to 49.6 minutes for GreenLight) then GreenLight would become cost-incurring. Similarly, if the length of hospital stay following TURP or HoLEP reduced below 1.5 and 0.9 days respectively (relative to 1.6 days for GreenLight) then GreenLight would become cost-incurring. However, as existing clinical coding is unable to distinguish GreenLight from HoLEP laser procedures (from where the 1.6 days length of stay was derived from) there remains uncertainty regarding length of stay across all arms."*

Issue 7

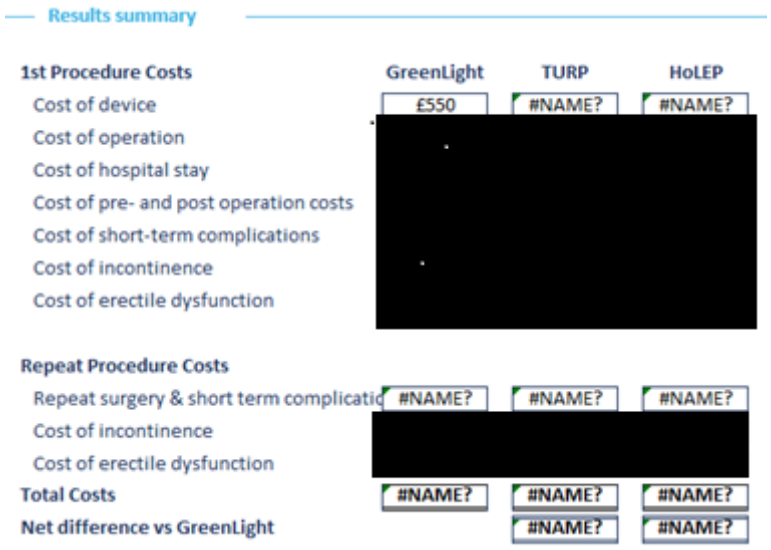
Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pages 102,108-111,132,135, 137-142,144 GreenLight total cost of consumables: £540	To align with the costing methodology recommended by the EAC (i.e., basing costs on the original Rezum assessment (MTG49)), GreenLight total cost of consumables should be updated to £500 [redacted]. Alternatively, this can be run as	The EAC for GreenLight 2022 took the price of £540 from the MTG49 (Rezum Evaluation) and noted that they preferred that the unit costs of the consumables for all	Thank you for your comment. The EAC note the cost of GreenLight used by the Company in the updated Economic model was £550. We have added a scenario to Table 25 of the assessment report to reflect the

	a scenario analysis and quoted in the executive summary.	technologies were extracted from the same source. The cost of £540 was derived by the EAC for Rezum under MTG49, noting the following "The cost of GreenLight was £550 in the MTG29 model. This reflects the current list price and has not been inflated using the CPI. The NHS supply chain lists a cost of £600 for a laser fibre HPS fibre (NHS Supply Chain, 2019). Minus VAT, this is £540". In April 2022, the Company verified the price under NHS Supply Chain with email correspondence from NHS Supply Chain and was told NHS supply chain lists a cost of [redacted] This discrepancy between the cost quoted in 2022 and used in MTG49 may be either due to the application of an incorrect VAT rate or a change in the VAT rate between these two time points.	reduced cost of £500 as recommended by the Company in this comment. The executive summary remains unchanged.

Issue 8

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 111 *"From threshold analysis (when maintaining GreenLight day-case procedures at 68%), the proportion of day-case procedures for TURP would have to exceed 43.6% before GreenLight would be considered cost-incurring, Figure 1; this is clinically unlikely."* Page 145 *"If more than 43.6% of TURP procedures or more than 56% of HoLEP procedures were conducted as day-case procedures, then GreenLight becomes cost-incurring if the proportion of GreenLight procedures conducted as a day-case remains fixed at 68%."*	We propose the following amendments: Page 111 *"From threshold analysis (when maintaining GreenLight day-case procedures at 68%), the proportion of day-case procedures for TURP would have to exceed 43.6% before GreenLight would be considered cost-incurring, Figure 1; this is clinically unlikely as TURP routinely requires overnight admission. Clinical experts accepted the assumption that TURP is performed as a day-case in only 4% of cases."* Page 145 *"If more than 43.6% of TURP procedures or more than 56% of HoLEP procedures were conducted as day-case procedures, then GreenLight becomes cost-incurring if the proportion of GreenLight procedures conducted as a day-case remains fixed at 68%." However, TURP routinely requires overnight admission therefore this scenario is clinically unlikely.*	These adjustments provide further context for why this scenario is clinically unlikely.	Thank you for your comment. Not a factual inaccuracy. No change required. The EAC also note that three of ten Clinical experts agreed that 4% of TURP can be performed as a day-case procedure, three noted that 4% would be a lower estimate with up to 20% suggested. Two experts also noted that some centres have higher volumes of TURP day-case procedures with one centre noting a 71% day-case rate. Two were unable to comment or were unsure (EAC Correspondence Log, 2022).

Issue 9

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 114 *"The updated model (provided in Microsoft Excel) was only partially executable (Visual Basic errors required debugging, a number of cells contained "?NAME" or "N/A" errors when modelling some scenarios)."*	We propose to adjust this sentence as follows: *"Minor errors were identified in the model submitted (Visual Basic errors required debugging, a number of cells contained "?NAME" errors when modelling a small number of scenarios)."*	The term "partially executable" is not appropriate and suggests that the model submitted was not valid which is inaccurate. On submission, for the scenarios being considered (high-risk population) there were no VBA errors identified by the manufacturer. The model was checked internally and externally, and the results were deemed repeatable. The EAC identified a small number of errors ("?/NAME") when running scenarios that the company were not expecting to be considered including adding erectile dysfunction. These errors were quickly corrected with an explanation provided by the manufacturer. Note that the term 'N/A' used in the model refers to 'Not Applicable' and is not an error.	Thank you for your comment. The EAC has stated partially executable as they could not use the Excel model to replicate results from the updated submission. The EAC has refrained from using subjective statements (such as "minor"). When opening the model and changing the "High-risk" setting to "No", we obtain the following output. No changes to report made. 

Issue 10

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 115 *"The updated model (version 2) remained only partially executable. The EAC sent an additional list of queries to the Company (on 04/04/2022) after it identified a number of discrepancies between the Submission and model, and between worksheets within the model (EAC Correspondence Log, 2022)."*	We propose to adjust this sentence as follows: *"The EAC sent an additional list of queries to the Company (on 04/04/2022) after it identified a small number of discrepancies between the Submission and model, and between worksheets within the model (EAC Correspondence Log, 2022). Queries raised by the EAC were answered and errors promptly amended by the manufacturer."*	The term "partially executable" is not appropriate. The company endeavored to respond to questions raised by the NICE EAC team promptly, in a short, unplanned time frame. The discrepancies were minor typographical errors and were due to changes made with haste to comply with the timelines requested by the EAC.	Thank you for your comment. This is not a factual inaccuracy. Timelines were set by NICE not the EAC. The EAC has refrained from using subjective terms throughout the report. Version 2 of the model remained partially executable as described in response to Issue 9. Questions submitted to the company and responses (including the date they were received) are described explicitly in the EAC Correspondence Log, 2022. No changes to the report made.

Issue 11

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 116 *"The EAC remain unclear why the Company has restricted to a four-year timeframe when data are available across all arms up to five years."*	We propose to replace this sentence as follows: *"The company stated that the model submitted applied the same structure and assumptions as the model reviewed under MTG49, which applied a 4 year time horizon. The EAC updated the model to account for 5-year data which is now available."*	The current phrasing is misleading as the rationale was provided. The company stated in the accompanying documents that the submission used the model submitted for MTG49. The only structural changes made were to allow a high-risk population to be considered easily within this model.	Thank you for your comment. The EAC has changed this wording to the following: "The Company model used a 4-year time horizon for consistency with the model submitted for Rezum (MTG49) which only had 4 year follow-up data available. The EAC notes that 5-year follow-up data are available for GreenLight."

Issue 12

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 118, Table 22 *"This assumption is not explicitly stated within the updated Company Economic Submission although remains in the assumptions tab within the submitted model."*	We propose to amend this sentence as follows: *"The assumption replicates the economic model submitted to MTG49."*	The current phrasing is misleading as the rationale was provided. The company stated in the accompanying documents that the submission used the model submitted for MTG49 which documents the assumption and the rationale.	Thank you for your comment. This is not a factual inaccuracy as the rationale and assumption was not explicitly stated within the documents submitted for this Assessment Report update (MTG 564). The EAC had stated on page 117 "The Company noted that the same assumptions underpinning the original Rezum economic model submitted to NICE (within MTG49) were applied in the updated model for GreenLight". The EAC have also added this clarification in Table 22, row 3 column 4.

Issue 13

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 118, Table 22 *"The input value primary sources were not explicitly reported in the updated Economic Submission or within the unpublished systematic review so it is not clear to the EAC where the input parameters have been derived from and so*	We suggest the following wording, as it is misleading to state that input sources were not reported in the economic submission. Page 118 *"The input value primary sources were not explicitly reported in the unpublished systematic review so it is not clear to the EAC where the input parameters have been derived from and*	Page 118 This is not correct; all input sources were clearly stated within the economic model. Page 122 We appreciate that the EAC will have been working under time and resource constraints that limited how far it was able to review the	Thank you for your comment. The EAC accept that the Company submitted unpublished review contained a list of over 100 papers that contributed to the report, however the source papers contributing to each outcome was not explicitly reported. For example, 16 studies contributed to mean PVR over time (up to 60 months) for GreenLight 180 W XPS, 34 studies contributed to

cannot be easily verified or critically evaluated." Page 122 *"Updated clinical parameters were taken from the Company submitted systematic review; however, as the systematic review did not explicitly report which studies contributed to each outcome, the EAC was unable to verify the model input parameters."*	*so cannot be easily verified or critically evaluated."*	papers identified in our systematic review, however a full list of included papers was given in the report. We have collated a list of all studies that reported data for each outcome to clarify this and are able to provide this list to NICE and the EAC if it would be helpful.	TURP (monopolar, bipolar or unspecified). It was unclear to the EAC whether all studies were included derive the values reported at each time point and applied within the Economic modelling, particularly due to the acknowledged heterogeneity in follow-up periods and few studies reporting outcomes to this timeframe. The EAC have amended row 1 to state: "The systematic review did not explicitly report which studies contributed to each outcome, therefore the EAC was unable to verify the model input parameters."

Issue 14

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 120, Table 22 *"The Company have included a retreatment rate of 14.6% at 5.2 years in high-risk patients receiving HoLEP within their economic model; as derived from the unpublished systematic review. The primary sources for these figures were not explicitly reported for the EAC to verify. Four of seven Clinical experts suggest that HoLEP has the lowest retreatment rates and were unsure why this would be the*	We propose the following amendments: Page 120, Table 22 *"The Company have included a retreatment rate of 14.6% at 5.2 years in high-risk patients receiving HoLEP within their economic model; as derived from the unpublished systematic review. On further review the company have identified that this was due an error in the data extraction, and the upper bound for the HoLEP studies should be 3.3%, with a mid-point of 1.65% instead of 14.6%. Furthermore, the follow-up time should have also been 5 years*	We apologise as this appears to be a mistake in the data extraction. The upper bound value here comes from Krautschick et al. (1999) which is reporting on a neodymium laser intervention and should have been excluded from the review. This study has been removed from the updated SLR. The upper bound for the HoLEP studies should be 3.3%, and the mid-point 1.65%.	Thank you for your comment. This is not a factual inaccuracy. The EAC and Clinical experts reviewed the data presented to them with the unpublished systematic review. The value of retreatment rate in the HoLEP arm for the high-risk was challenged and considered implausible; the Company has now confirmed that this was an error in their updated model and Economic submission. This has no impact on the results of Table 25, where the EAC applied univariate changes when modelling all patients (High-risk setting

highest value in high-risk patients (EAC Correspondence Log, 2022).” Page 126, Table 23 *“HoLEP* *14.6%,* *5.2 years* *[N=6 studies; range: 0% to 29.2%]* *One Clinical expert stated that the proportions in the “high-risk” population do not make sense clinically (EAC Correspondence Log, 2022). The expert stated that it was not clear why reintervention rate would be the highest for HoLEP in a high-risk population, as it would be expected to have the lowest (EAC Correspondence Log, 2022).”* Pages 123, 145 All relevant text reporting this inaccuracy in HoLEP retreatment rate	*rather than 5.2 years to be consistent with the other retreatment data extracted from literature review. The primary sources for these figures were not explicitly reported for the EAC to verify. Four of seven Clinical experts suggest that HoLEP has the lowest retreatment rates (EAC Correspondence Log, 2022), and this aligns with the updated rates provided by the company.”* Page 126, Table 23 *“HoLEP* *1.65%,* *5 years* *[N=5 studies; range: 0% to 3.3%]”* Please amend all text reporting this incorrect retreatment rate for HoLEP, (including clinical validity conclusions drawn from this inaccuracy) accordingly, to reflect the above correction.	This updated reintervention rate for HoLEP is now aligned with clinical expert opinion. We have collated a list of all studies that reported data for each outcome and are able to provide this list to NICE and the EAC if it would be helpful.	changed to “No”), where retreatment rate for HoLEP is set to 0%.

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Issue 15

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 122 *"This systematic review reported outcomes from more than 100 studies, which included GreenLight XPS as well as other BPH surgical interventions, and where more than half of the recruited population were classified as high-risk."* Pages 123, 287-290, 292-297 (Table B4.1), 307-310 (Table B4.3) All relevant text relating to this inaccuracy	We propose the amendment of this sentence to correct this assumption as follows: *"This systematic review reported outcomes from more than 100 studies, which included GreenLight XPS as well as other BPH surgical interventions, and where either 100% of the recruited population were classified as high-risk, or where relevant data was reported for a high-risk subgroup within a mixed population."* Please amend all text reporting this inaccuracy, (including conclusions drawn from this inaccuracy) accordingly, to reflect the above correction.	This is not true. This assumption has been made due to an ambiguity in the reported methodology of the systematic review submitted to NICE, for which we apologise. Due to the amount of evidence available the authors did not include any studies with a mixed population unless there was a sub-group analysis for only the high-risk population. Data was only extracted where either 100% of the recruited population were classified as high-risk, or where relevant data was reported for a high-risk subgroup within a mixed population.	Thank you for your comment. The EAC appraised the submitted systematic review on the basis that the stated inclusion and exclusion criteria set out in Table S4: "mixed populations where <50% of the participants are high-risk and where the data is not reported separately". The EAC are unable to verify or critically appraise the application of the inclusion and exclusion criteria as the input source for each outcome was not explicitly reported within the unpublished systematic review submitted to the EAC. The EAC note that one of the included studies (Azizi *et al.* 2017) within the unpublished systematic review identified as exclusively in patients with large prostates included patients with a *mean* volume greater than 80 ml within Table S5. The EAC have made changes on page 123-4 and within Appendix B4 of the Assessment Report Update to clarify the interpretation of the inclusion and exclusion criteria.

Issue 16

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 123 *"The systematic review missed a number of eligible studies (identified by the EAC during its independent literature review) which included high-risk patients."* Page 289 *"The EAC would consider that two studies meet the eligibility criteria and were published before the search date and therefore should have been included in the systematic review (Hibon et al. 2017 was identified by the Company but excluded due to "no relevant data", and Akhtar et al. 2018 was not identified)."* Page 290 "*As the systematic review missed eligible studies …"*	We propose that these statements be removed.	Most of the papers identified by the EAC were either published since the search date or were excluded from the systematic review for not reporting data on a high-risk subgroup. The EAC identified two studies that they consider meet the eligibility criteria and should have been included in the systematic review. (Hibon et al. 2017 and Akhtar et al. 2018). Hibon et al. 2017: This study was excluded at full-text screening as no data was reported for the high-risk subgroup. Akhtar et al. 2018: This study was not identified by the search, however no data was reported for the high-risk subgroup so it would have been excluded had it been identified. The EAC has not demonstrated that any relevant studies that met the inclusion criteria were missed. Given the prior considerations made by the EAC were based on a misunderstanding of inclusion	Thank you for your comment. The EAC appraised the submitted systematic review on the basis that the stated inclusion and exclusion criteria set out in Table S4 and have identified the studies 'published after the systematic review search dates'. The paper by Hibon *et al.* (2017) included patients where mean prostate volume was greater than 80 ml, which appears to be how the inclusion and exclusion criteria has been applied in other studies within Table S5. The paper by Akhtar *et al.* (2018) reported complication outcomes for patients considered high surgical risk and intraoperative parameters (lasing time, energy used, fibres used) by subgroups based on prostate size (<80 ml, >80ml) and would be appropriate to include based on the inclusion and exclusion criteria set out in Table S4. The EAC have amended the assessment report to state that the Company have clarified that only studies explicitly reporting on high-risk patients were included in the systematic review. The EAC has been unable to verify or critically appraise the application of the

		criteria, we hope the EAC will now agree that neither of these studies would meet the inclusion criteria to be included in the study.	inclusion and exclusion criteria or studies contributing to each parameter used in the Economic submission due to lack of reporting within the unpublished systematic review.

Issue 17

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 123 *"The systematic review also:* *•included conference abstracts (lacking peer-review);* *•included studies where only 50% or greater of the included patients were high-risk;* *•was not transparently reported such that the EAC was unable to verify outcomes;* *•some model inputs (for example, retreatment rates) lacked clinical validity as highlighted by the Clinical experts (EAC Correspondence Log, 2022);* *•acknowledged large heterogeneity across included studies preventing meta-analysis;* *•was subject to bias and substantial conflict of interest as*	We propose that these points be amended as follows: *"The systematic review also:* *•included conference abstracts (lacking peer-review);* *•was not transparently reported such that the EAC was unable to verify outcomes;* *•acknowledged large heterogeneity across included studies preventing meta-analysis;* *•was subject to potential bias and conflict of interest as a minority of its authors were employees of Boston Scientific.* *Therefore, the EAC would consider that the results of the unpublished systematic review are subject to uncertainty due to the heterogeneity of the data. No new published literature relevant to the scope was identified in the latest Economic Submission."*	*"•included studies where only 50% or greater of the included patients were high-risk;"* This is not true. This assumption has been made due to an ambiguity in the reported methodology of the systematic review submitted to NICE, for which we apologise. Due to the amount of evidence available the authors did not include any studies with a mixed population unless there was a sub-group analysis for only the high-risk population. Data was only extracted where either 100% of the recruited population were classified as high-risk, or where relevant data was reported for a high-risk subgroup within a mixed population. We suggest removing this statement as it is not accurate.	Thank you for your comment. The EAC appraised the submitted unpublished systematic review on the basis that the stated inclusion criteria were accurate. Clinical experts also queried the large difference in retreatment rates between mono- and bi-polar TURP as noted in response to Issue 14. The EAC has added additional text to explicitly state the involvement of Boston Scientific within the unpublished systematic review: • was funded by Boston Scientific; • declared conflicts of interest as 3 authors being employees of Boston Scientific, 2 receiving funding from Boston Scientific to conduct the research, 3 worked

the majority of its authors were employees of Boston Scientific. *Therefore, the EAC would consider the unpublished systematic review as low quality and the results as not robust. No new published literature relevant to the scope was identified in the latest Economic Submission."*		*"•some model inputs (for example, retreatment rates) lacked clinical validity as highlighted by the Clinical experts (EAC Correspondence Log, 2022);"* If the EAC accept the updated re-treatment rates, this comment is now redundant, and we therefore suggest it be removed. *"•was subject to bias and substantial conflict of interest as the majority of its authors were employees of Boston Scientific."* The above statement is misleading. Although Boston Scientific have supported and contributed to the development of the systematic review as subject matter experts, it was conducted by an independent company using the methodology recommended by NICE. The unpublished systematic review lists eight authors, of which three are employees of Boston Scientific. This does not represent a majority and should be re-worded to reflect this. We would also argue that most if not all manufacturers' submissions to NICE are supported by SLRs that were funded by the manufacturer.	as a consultant for Boston Scientific. The EAC appraised the unpublished systematic review as it was submitted in line with the timeline set by NICE. Not a factual inaccuracy, no change made to the report.

		"Therefore, the EAC would consider the unpublished systematic review as low quality and the results as not robust. No new published literature relevant to the scope was identified in the latest Economic Submission." The EAC have valid questions with regards to the systematic review which we believe we have now addressed, and as a result we hope that the EAC will recognise that the quality of the SLR is greater than they first thought. The manuscript did not specify which papers contributed data to each outcome for reasons of space, but this information is now available and can be shared if requested. The SLR was conducted following the requirements set out by NICE. We believe that it is important to differentiate the quality of the SLR, which we do not believe is of low quality, from the substantial heterogeneity of the studies identified by the SLR, which we have acknowledged leads to uncertainty in drawing conclusions.	

Issue 18

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 133 *"The EAC would consider that the addition of the high-risk scenario has reduced the transparency of the economic model, and introduced errors into the model."*	Remove and replace with: *"The EAC did not consider the high-risk population because of uncertainty around the clinical data."*	No changes were made to the economic model other than adding the high-risk population which was intended to make it easier for the EAC to modify data specific to the high-risk population. The errors identified were very minor and related to back-end sheets intended to extract the data for reporting and were not applicable to the average risk population. This statement is therefore inappropriate.	Thank you for your comment. Not factual inaccuracy. Errors identified were noted within the modelling of all patients, see Appendix E3 of the Assessment Report Update. No change to report made.

Issue 19

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 133 • *"despite the clinical parameters when modelling all patients matching those of the original Rezum model, differences in PSA parameters were identified*	These two points should be stated independently rather than as a bullet under a statement stating that there were errors in the submission.	Differences in PSA results obtained from two different models may be due to a wide range of factors. This discrepancy is unlikely to be related to the addition of the high-risk population.	Thank you for your comment. This is not a factual inaccuracy, the bullet points refer to the errors identified within the PSA of the updated Company model. The EAC have added clarity to note that discrepancies in the model were noted in both the modelling of all patients and

between the two (Appendix E3), • *PSA distribution errors identified in the original Rezum economic model (Appendix E of the Rezum Assessment Report, 2019) have been corrected in the updated model for mono-TURP, bi-TURP, and HoLEP arms, with errors remaining for GreenLight, when modelling all patients."*		The second point is not related to the addition of the high-risk population.	high risk patients with "The EAC *also* noted several discrepancies in the model resulting in the EAC being unable to replicate the PSA of the updated Company model, including: ".

Issue 20

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 142 *"Additionally, the Company revised model (version 2) developed in Microsoft Excel was only partially executable, therefore the the EAC replicated the Company base case model (all patients) using R programming language (R Core Team, 2020) and the rdecision package (version 1.1.0)."*	Adjust this sentence as follows: *"To validate the model results, the EAC replicated the Company base case model (all patients) using R programming language (R Core Team, 2020) and the rdecision package (version 1.1.0)."*	The term "partially executable" is not appropriate for the reasons detailed in Issues 10/11.	Thank you for your comment. See above response (Issue 9).

Issue 21

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 290 *"The main limitations of this review are the potential risk of bias and conflicting interest due to the systematic review being funded by Boston Scientific (the manufacturer of the GreenLight device), with three out of eight authors being directly employed and two authors funded to conduct the research by Boston Scientific. The remaining three authors have worked as consultants for Boston Scientific. The study acknowledges seven individuals who assisted in conducting abstract screening and data extraction with affilliations not stated."*	We propose the following amendments to this paragraph: *"A limitation of this review is the potential risk of bias and conflicting interest due to the systematic review being funded by Boston Scientific (the manufacturer of the GreenLight device), with three out of eight authors being directly employed and two authors funded to conduct the research by Boston Scientific. The remaining three authors have worked as consultants for Boston Scientific. The study acknowledges seven individuals who assisted in conducting abstract screening and data extraction with affiliations not stated."*	We contend that these conclusions are based on factual inaccuracies that we have addressed in Issue 17 and would therefore ask the EAC to amend accordingly.	Thank you for your comment. The EAC has amended page 290 and page 120 to describe conflicts of interest and funding for the unpublished systematic review. Author affiliation is not a source of bias.