National Institute for Health and Care Excellence

Medical technologies evaluation programme

MT 413 Rezum for treating lower urinary tract symptoms secondary to benign prostatic hyperplasia

Consultation comments table (internal teams, committee & EAC)

There are 98 consultation comments from 10 consultees, including 71 specific comments about the draft guidance (3 duplicates) and 27 comments to the consultation questions:

- 6 NHS professional including 5 urologists
- 1 manufacturer (sponsor)
- 1 manufacturer (other)
- 1 layperson
- 1 national organisation

The comments are reproduced in full, including in the following themes:

- Draft recommendations and the rationale (comments 1 to 15)
- Patient selection and indication (comments 16 to 18)
- Technology description (comments 19 to 25)
- Clinical evidence (comments 26 to 51)
- Cost modelling (comments 52 to 72)
- Side effects (comment 73 to 84)
- Others (comments 85 to 96)
- Research (comment 97 to 98)

Comment no.	Consultee ID	Group	Section	Comments	NICE response DRAFT guidance

Draft recommendation (n=15)					
1	9	NHS professional	Recommendation 1.2	Agree on the size criteria. Prostates larger than 80cc should not be offered Rezum and should be offered instead NICE approved alternative treatments such as the Holmium Laser Enucleation of the Prostate (HoLEP) which is more suitable for larger prostates.	Thank you for your comment. The committee agreed that Rezum should be used for people with moderate to severe LUTS due to BPH with an estimated prostate volume of between 30 and 80 cm^3 (see section 4.2).
2	9	NHS professional	Recommendation	Rezum should not be offered at this stage for patients in urinary retention as the current evidence still does not support this. Retention patients were excluded from the Pivotal trial. For this group of patients other treatments such as TURP or HoLEP should be considered.	Thank you for your comment. The committee considered your comment carefully and acknowledged that the Rezum II study excluded people with urinary retention. The committee considered that future research would be valuable to assess the efficacy of using Rezum treating BPH in people with urinary retention (see section 4.15).
3	6	Manufacturer (other)	Recommendation 1.2	The recommendations that Rezum can be done under a local anaesthetic or light sedation does not reflect actual NHS practice. In the results of a Patient Questionnaire, provided in the MT413 Rezum Supporting documentation – Committee papers, 75% of patients had a general anaesthetic. In the Adoption Scoping Report, also in the Supporting Documentation, the 9 Urologists who were consulted (7 of which use Rezum) said the method of anaesthesia was general anaesthetic, sedation with local anaesthetic or spinal block.	Thank you for your comment. The committee considered your comment carefully and, based on experts' advice, acknowledged that around two thirds Rezum procedures were done using a general anaesthetic, but the procedure can also be done using a local anaesthetic with sedation. The choice of anaesthetic varies depending on the patient preference and service provision in hospitals (see section 4.8). The committee decided to remove the reference to the use of local anaesthesia in section 1.2 and to amend the wording in section 4.8 to note the use of general anaesthetics in clinical practice and that it can also be done under a local anaesthetic with sedation.
4	7	NHS professional	Recommendation 1.2: Rezum is a minimally invasive procedure and can be done under local	I'd say that Rezum really is mostly done under general anaesthetic. I am not aware of anyone in the UK doing this regularly under local.	Thank you for your comment. Please see the response to comment 3.

			anaesthesia or light sedation		
5	8	NHS professional	Recommendation 1.2: and can be done under local anaesthesia or light sedation	It is likely that most patients in the UK will either receive a short general anaesthetic or IV sedation given safely by an anaesthetist (just as they currently do with Urolift). Very few indeed will be only under local anaesthetic	Thank you for your comment. Please see the response to comment 3.
6	1	NHS professional	Recommendation 1.3: Cost modelling estimates that, per person over 4 years, Rezum is cost saving compared with	I think there needs to be further costing analysis incorporating the actual cost to the NHS and tax-payer. This is the HRG for which each procedure is charged to commissioners. It appears that the newer interventions attract a higher HRG. Also this needs to be offset by the costs of re-intervention and other treatment costs	Thank you for your comment. The committee considered your comment carefully and acknowledged that the economic model estimates the actual absolute and incremental cost of the technology to the NHS and PSS. This is standard process during guidance development as described in the MTEP methods and process guides. If positive recommendations are published NICE resource impact (RIA) team assesses the impact of the use of Rezum on NHS resource use. For providers, the cost would be £1,348 to perform the Rezum procedure. The cost of the device and consumables of Rezum is higher than when compared to some of the existing surgical treatment options. However, any additional the cost of consumables to providers, should be offset by an increase in income because of the benefits from productivity gains as a result of shorter theatre times and a reduced length of stay when using Rezum. The resource impact of implementing this guidance is not expected to be significant. The committee decided not to change the guidance.
7	7	NHS professional	Rationale: Rezum is associated with improved quality of life and preserved sexual function	When comparing Rezum with Urolift it is only Urolift that has been shown to cause no de novo sexual dysfunction, and this needs to be clear to patients.	Thank you for your comment. The committee considered your comment and the available evidence carefully. It agreed that Rezum has very little negative effect on erectile dysfunction, but can cause reduced ejaculation volume or, rarely, anejaculation, in some individuals.

					The committee decided to make minor amendments to the guidance (the rationale, section 3.2 and 4.3) to clarify a low risk affecting sexual dysfunction after Rezum.
8	8	NHS professional	Recommendation 1.1	In the absence of a randomised controlled trial against another treatment it is not reasonable to come to this conclusion. It appears better than 'sham' treatment at 3 months is the only strong conclusion and even then 2/3 of the 'sham' patients guessed they had received sham	Thank you for your comment. The committee considered the comment and the available evidence carefully. It agreed with the lack of direct comparative evidence and concluded that further research to address the efficacy of Rezum compared with other surgical interventions would be welcome (see section 4.15).
9	1	NHS professional	Consultation question	*Are the recommendations sound and a suitable basis for guidance to the NHS?* Yes except for the costing caveat previously raised	Thank you for your comment. Please see the response to comment 6.
10	2	NHS professional	Consultation question	*Are the recommendations sound and a suitable basis for guidance to the NHS?* Some men with IPSS score less than 13 but on medication that they wish to stop and cannot tolerate are also eligible for Rezum.	Thank you for your comment. The committee considered the comment and the clinical experts noted that Rezum is one of treatment options for people with LUTS due to BPH, and the treatment options vary in clinical practice depending on an assessment of individuals' symptoms, patients' preference and the availability of service provision.
11	4	NHS professional	Consultation question	*Are the recommendations sound and a suitable basis for guidance to the NHS?* Agree	Thank you for your comment.
12	5	Lay person	Consultation question	*Are the recommendations sound and a suitable basis for guidance to the NHS?* I am a layperson that has been treated with the Rezum system. I am a citizen of the United States of America. I greatly appreciate the opportunity to make these comments. I have friends in the United Kingdom. I hope that they can benefit from my comments and any action by the NHS.	Thank you for your comment and sharing your experience.
13	8	NHS professional	Consultation question	*Are the recommendations sound and a suitable basis for guidance to the NHS?* No - I believe it would be dangerous to extrapolate these data into widespread NHS practice without proper RCTs.	Thank you for your comment. The committee considered the comment and available evidence carefully. It agreed that the evidence was mainly based on one pivotal study (Rezum II trial) and

					included studies were done outside the UK. Nonetheless, the clinical experts explained that the study population included in the Rezum II study is similar to the people that they treat with Rezum in their own practice in the NHS. The committee concluded that the evidence is generalisable to UK NHS practice. In addition, the committee acknowledged the evidence gap in current evidence base due to a lack of comparative evidence on Rezum and other treatments for BPH, and considered further research would be value to improve the evidence base (see section 4.15).
14	9	NHS professional	Consultation question	*Are the recommendations sound and a suitable basis for guidance to the NHS?* Yes	Thank you for your comment.
15	10	Representative of national organisation	Consultation question	*Are the recommendations sound and a suitable basis for guidance to the NHS?* The opinion of the EAU Guidelines panel is that further RCTs against a reference technique are needed to confirm the clinical results and to evaluate mid- and long-term efficacy and safety of water vapour energy treatment. NIHR are currently considering applications for a comparative RCT and in our opinion there is currently not enough evidence to support the widespread adoption of this technique throughout the health service. We are acutely aware of the issues created by the widespread adoption of mesh implants and believe there needs to be a strong evidence base to support the adoption of novel techniques.	Thank you for your comment. The committee considered the comment and acknowledged the evidence gap in current evidence base on Rezum and other treatments for BPH. The committee agreed that further research would be valuable to improve the evidence base (see section 4.15).
Patient selection (n=3)					
16	2	NHS professional	General	Overall, I support the recommendations in this document. In my practice and centre at Imperial, probably the largest in the UK, we have found it to be effective in the vast majority of cases and has allowed us to conduct more cases for the equal time that a TURP or laser would take. This has enabled us to reduce waiting times. I wish to make a few points:	Thank you for your comments and for sharing your clinical experience. The committee considered your comment carefully. It noted that for the 2 treatments using laser: HoLEP was modelled with a hospital stay of 2 days and Green light was modelled with an average of 0.7 days

				- The procedure can often be done in men in retention and cases series and our experience shows 70-80% are able to get catheter free. Many of the others have dysfunctional hypocontractile bladders and would not be catheter free even with a TURP. - I do not think the assumption that laser TURP patients go home the same day across the UK is true. Most stay an overnight stay with only very expert centres sending their morning patients home only. The economic model is therefore unnecessarily weighted towards laser TURP and the economic argument could be much more favourable as the document has recognised. - Men with mild LUTS IPSS <13 with medication sometimes cannot tolerate medication or the side-effects are sufficiently bad that they wish to have something. This should be an indication as patients should have the choice to be able to come off medication. - prostates larger than 80cc could have Rezum but the effectiveness is limited; offering a period of cytoreduction for 4-6 months for glands up to 110cc and then carrying out the Rezum would be appropriate in those men who wish to have this option.	(95% CI 0.5 to 0.8) hospital stay, based on data from an observational study (Ajib et al. 2018). Cost modelling in MTG27 for GreenLight assumed 36% of procedures are day cases. The committee was aware that GreenLight hospital stay is a source of uncertainty as described in the assessment report (section 9.2.4 page 70). Please see the responses to comment 1 and 10.
17	5	Lay person	Section 4.9: Rezum is used to treat patients with benign prostate enlargement but there is no consensus on how to measure prostate size	Even if their was consensus on how to measure the size of the prostate, the instructions for use of the Rezum device DO NOT require that the size of the prostate be considered in administering the Rezum treatments. This is illogical.	Thank you for your comment. The committee considered your comment carefully and noted that the instructions for use states that Rezum is indicated for men with a prostate volume 30cm^3 or more, and the clinical experts advised that, in clinical practice, treatment decision is based on individuals' factors and the availability of service. The committee decided not to change the guidance.
18	4	NHS professional	Section 4.2: Symptoms Score (IPSS) of 13 or greater, and with a prostate volume, measured by transrectal ultrasound, of 30 cm3 to 80 cm3.	Speaking as a urologist from a centre serving an elderly population, there is a large proportion of patients, whose clinical parameters fall outside the mentioned cutoff for the prostate size. Additional research is urgently required to look at the performance of the procedure in larger prostates and in urinary retention, as these patients request the treatment and also highly suitable for it due to presence of comorbidites (so unfit for TURP).	Thank you for your comment. The committee considered your comment carefully and agreed that there is little evidence for using Rezum in these groups of the population. It decided to include a comment about the value of future research to assess the efficacy of using Rezum for treating BPH in people with

					large prostate and urinary retention (see section 4.15).
The technology description (n=7)					
19	9	NHS professional	Section 2: The technology	In the Intended Use section: Should read as "volumes greater than 30cc and less than 80cc". Specifying the upper limit prostate size cut-off is extremely important. Prostates larger than 80cc should be offered a HoLEP.	Thank you for your comment. The committee considered your comment carefully and acknowledged that the UK version of Instruction for use (IFU) does not specify the upper limit prostate size cut off while the US version IFU specify the use of Rezum for prostate size between 30 and 80 cm^3. This was discussed with the company during the evaluation. The committee decided not to change the guidance.
20	1	NHS professional (commissioner)	Section 2: The typical consumable cost of the Rezum procedure is estimated at £1,348 (excluding VAT) per treatment.	This cost is a bottom up costing incurred by providers, as opposed to the actual cost charged to commissioners under Payment by Results which should also be reflected.	Thank you for your comment. Please see the response to comment 6.
21	6	Manufacturer (other)	Section 2: The procedure is done under local, regional or general anaesthesia	The recommendations that Rezum can be done under a local anaesthetic or light sedation does not reflect actual NHS practice. In the results of a Patient Questionnaire, provided in the MT413 Rezum Supporting documentation – Committee papers, 75% of patients had a general anaesthetic. In the Adoption Scoping Report, also in the Supporting Documentation, the 9 Urologists who were consulted (7 of which use Rezum) said the method of anaesthesia was general anaesthetic, sedation with local anaesthetic or spinal block.	This is a duplicate. Please see response to comment 3.
22	8	NHS professional	Section 2: or	or sedation,	Thank you for your comment. The last sentence in section 2 (technology) has been amended to include local anaesthesia with sedation in the list of anaesthesia options for the Rezum procedure.
23	8	NHS professional	Section 2: central	middle or median lobe would be more usual	Thank you for your comment. The last sentence in section 2 (innovative aspects) has been amended to state that Rezum

					can be used to treat both the median or middle lobe of the prostrate.
24	8	NHS professional	Section 2: £1,348	Is this the cost of the single use device itself or for all the consumables required?	Thank you for your comment. The EAC confirmed that the cost £1,348 per treatment includes all the consumables. The generator is provided by the company free of charge (including training and maintenance).
25	5	Lay person	Section 4.2 Rezum should be used for men with moderate to severe LUTS with an estimated prostate volume of 30 cm3 to 80 cm3	The clinical trial is not entirely clear on the point, but it appears that in all cases a limited number of Rezum treatments were provided to the study participants. It appears that no clinical trial participants received a large number of Rezum treatments, such as the fifteen (15) I received. The Rezum device can deliver this maximum number of treatments but the criteria for administration of higher numbers of treatments is not supported by the clinical trial experience.	Thank you for your comment. The committee considered your comment carefully, and noted that the instruction for use states the single delivery device can perform up to 15 injections. The EAC reviewed all included studies, some of which reported the number of injections used: • The Rezum II trial,.a mean of 4.5 (±1.8 SD) 9 second steam injections were applied.. • Mollengarden reported 5.5 ± 2.1 injections during the Rezum procedure. • Dixon reported 4.6 injections (range 2 to 9). • Darson reported 4.4 injection (range 2 to 12). Therefore most patients in the included studies received between 4 and 5 injections. The clinical experts advised an average of 6 to 7 injections are used in their experience. Currently there is no evidence on the association between the number of steam injections and their associated side effects, and the committee agreed to add a research consideration noting the potential value of this information (see section 4.15).
Clinical evidence (n=26)					
26	1	NHS professional	Consultation question	*Has all of the relevant evidence been taken into account?* As far as I am aware	Thank you for your comment.

27	2	NHS professional	Consultation question	*Has all of the relevant evidence been taken into account?* There is a case series on men who have had Rezum following retention. Holland BC, Gupta N, Delfino K, et al. Convective radiofrequency water vapor energy prostate ablation (Rezum) effectively treats urinary retention. [abstract] J Urol 2017;197(4S):e337. Poster presented at the American Urological Association 2017 annual meeting in Boston on May 13, 2017. Poster MP27-20."	Thank you for your comment and sharing the study. The EAC has reviewed the study provided a summary (see table 1 in appendix 1).
28	4	NHS professional	Consultation question	*Has all of the relevant evidence been taken into account?* It appears so	Thank you for your comment.
29	5	Lay person	Consultation question	*Has all of the relevant evidence been taken into account?* I am familiar with the Three-year and Four-year Rezum clinical trial studies as well as other evaluations of the Rezum system available through PubMed. In the spring of 2018 I was treated with the Rezum system.	Thank you for your comment.
30	8	NHS professional	Consultation question	*Has all of the relevant evidence been taken into account?* Yes but it is limited in quality and quantity	Thank you for your comment.
31	9	NHS professional	Consultation question	*Has all of the relevant evidence been taken into account?* Yes	Thank you for your comment.
32	10	Representative of national organisation	Consultation question	*Has all of the relevant evidence been taken into account?* Yes to a certain extent but the available evidence is insufficient to support the conclusions being drawn	Thank you for your comment.
33	10	Representative of national organisation	Consultation question	*Are the summaries of clinical and resource savings reasonable interpretations of the evidence?* Even if the risks of bias from the 1 RCT are ignored, it is a technique which is only applicable to men with a rather narrow range of inclusion criteria • men aged > 50 • IPSS ≥ 13, • Qmax ≤ 15 mL/s • prostate volume between 30 and 80 cc The technique would seem not to be suitable for men with big prostates and is unlikely to benefit men with severe BOO. Less than 15ml/sec is a poor surrogate for BOO. The results from the RCT should not be extrapolated to all patients.	Thank you for your comment. Please see the responses to comment 1 and 10.
34	6	Manufacturer (other)	Rationale: Evidence also shows that using Rezum is	Statements about preserved sexual function with Rezum are misleading based on the evidence and may mislead patients into making choices about treatment based on an	Thank you for your comments. The committee considered your comment carefully and acknowledged that the

			associated with improved quality of life and preserved sexual function	understanding that that their sexual function will definitely be preserved. All thermal ablation procedures, including steam, have shown collateral damage of the prostate that leads to sporadic loss of ejaculatory function. MTG529 does not consider this important side effect and in fact assumes it to be the same as UroLift, which is the only treatment for BPH to never have a patient to have lost ejaculatory function in any report. The Rezum data is similar to the prior thermal ablation procedures because the mechanism of action is the same. Collateral damage to the bladder neck, ejaculatory ducts, and/or tissue surrounding the veru montanum are all potential causes of inconsistent results. The Rezum II study report avoids stating that Rezum preserves ejaculatory function because it does not reliably do so. While mean MSHQ-EjD scores were stable and even showed some improvement, 2.9% patients completely lost function (anejaculation) and 2.9% experienced “reduced ejaculatory volume”. This is similar to the 3.1% anejaculation reported by Mollengarden et al in the real-world study of Rezum [Prostate Cancer Prostatic Dis. 2018 Sep;21(3):379-385]. It is inappropriate to report adverse events simply as mean scores, since this hides low rates. If incontinence were treated this way, we would not acknowledge the possibility for incontinence after HoLEP or TURP, since mean scores stay largely level. This collateral damage associated with thermal ablation can be increased with more aggressive ablation, as seen in a report from the Mayo Clinic. Yang et a, from the Mayo Clinic, reported 20% anejaculation after Rezum; this was presented at conference [Yang DY et al. Abstract presented at AUA conference. 2018. Poster UP3-33 Prevalence of Ejaculatory Dysfunction Following Rezum Prostate Ablation] and is described in a comparison of Rezum and UroLift [Kaplan SA. Demistifying less-invasive solutions for BPH. Urology Times. Sept 2019]. Ines et al conducted a more in-depth report of sexual dysfunction after Rezum, showing 17% anejaculation [Ines M et al. A retrospective review of the Rezum System: Treatment for	Rezum II study indicated that erectile or ejaculatory function did not significantly worsen after Rezum compared with sham group (measured by IIE-EF and MSHQ-EjD scores in the Rezum II study). The study reported that 4 men (2.9%) experienced anejaculation. This did not negatively affect MHSQ-EjD scores significantly. No patient in the Rezum II trial suffered erectile dysfunction. The study results were in line with the view of the clinical experts suggesting that erectile function is not impacted by Rezum but some patients (around 10%) experienced a decrease in the volume of ejaculate with a small proportion experienced dry ejaculation. The EAC also reviewed Mollengarden et al. (2017) which was included in the Assessment Report. This retrospective study reported 4 patients (3.1%) with retrograde ejaculation (all were Clavien Dindo grade I, requiring minimal intervention). An ED rate of 3.1% was also recorded, with 2 patients having Clavien DIndo grade 2 (requiring medication). The EAC reviewed the references noted in the comment and provided a brief description (see table 1 in appendix 1). The committee was advised that the interpretation of these references should be treated with caution as these studies were not peer reviewed publications and may be subject to bias. The committee decided to make minor changes in the guidance (see the rationale, section 3.2 and 4.3) to clarify there is a low risk to sexual dysfunction after treating with Rezum.

				benign prostatic hyperplasia in men with mild, moderate and severe lower urinary tract symptoms. NSAUA Sept 2019]. Many NHS patients elect to have UroLift treatment instead of more invasive treatments in order to preserve sexual function. To not warn these men that Rezum does not offer the same certainty is a disservice to patients in whom these outcomes are important.	
35	6	Manufacturer (other)	Section 4.1: Rezum is an effective minimally invasive procedure with clinical benefits, Rezum is more versatile than UroLift in treating different shapes of prostate, for example in men with an obstructive median lobe.	The Committee was not given the opportunity to consider a recently published study with Urolift, looking at use in patients with OML (MedLIFT study1), Rukstalis et al showed that treatment of OML shows a significantly greater effect on both IPSS (13.5 vs 10.6) and Qmax (6.4 vs 4.0 ml/s) [Rukstalis D et al. Prostate Cancer and Prostatic Diseases 2019;22: 411-419. What is significant about this is that MedLift was an FDA IDE extension of the L.I.F.T. randomised study, designed to examine safety and efficacy of PUL for treatment of obstructive middle lobes (OML). Inclusion criteria were identical to the LIFT study, except for requiring an OML. The MedLIFT study was not included for consideration in the comparison of Rezum with Urolift, which introduces the potential for clinical bias towards Rezum when comparing these two treatments in men with OML.	Thank you for your comment. The committee considered your comment carefully. The EAC provided a summary of the Medlift study (see the study summary in appendix 1) for the committee consideration. The committee agreed the study showed that UroLift was as effective at treating median lobe obstruction as lateral lobe obstruction. However, there is no direct evidence comparing Rezum with UroLift for treating men with obstructive median lobes. The committee decided to amend the guidance (see section 4.1) to state that Rezum is versatile in treating different shapes of prostate without referring to UroLift.
36	6	Manufacturer (other)	General	General comment: Whilst it is recognised that Urolift, as an established minimally invasive treatment for LUTS from BPH, is an appropriate comparator to Rezum, we ask the committee to consider whether the timing of its inclusion as a comparator in the Rezum guidance (GID-MT529) is appropriate? We understand that the comparator for technologies undergoing evaluation by MTEP is the 'standard of care'. We dispute whether Urolift would be considered the current standard of care. Also, in light of the fact that MTAC has recently decided to consider a standard update to the Urolift guidance to reflect changes in estimated costs to the NHS and new evidence with regard to clinical contexts, service delivery and treatment pathway. None of these changes are reflected in the development of the draft Rezum guidance and it is clear that important information for clinical and non-clinical decision makers contained in MTG529 when published will be immediately superseded and contradicted by	Thank you for your comment. The committee considered your comment carefully, and acknowledged that there are a range of treatment options including Rezum available in the NHS for people with symptomatic BPH that have not responded to conservative therapy. UroLift was included as a comparator in the decision problem for this evaluation as another minimally invasive option for this patient population. NICE published MTG26 on UroLift in 2015, and the guidance is updated 3 years after its publication. The recent review decision on the UroLift guidance is to update the guidance (please see UroLift guidance review decision

				information in the revised MTG26. The cost and clinical assumptions regarding Urolift that are used in the Rezum (GID-MT529) economic modelling are largely based on base case results in Urolift guidance (MTG26) published in 2015. As the guidance for Rezum will be finalised before the committee can consider the update for Urolift, planned for 2020, the Rezum guidance will not reflect current costs or NHS practice, which will be considered in the Urolift update. We would ask, therefore, that the committee consider whether it would be more appropriate to remove Urolift as a comparator in the guidance for Rezum (GID-MT529) and instead include Rezum as a comparator in the update of Urolift MTG26, due to take place in 2020, when a full appraisal of current costs, clinical practice and latest evidence for Urolift will take place. In any event, it is clear that Rezum will now need to be included as a comparator in the update of MTG26, which will require a new cost analysis and new evidence review more akin to producing new guidance than an update. This new guidance will inevitably contain different assumptions to MTG529 as it will be based on current evidence and NHS clinical practice, and evidence available from five years ago. The resultant outcome from these two interdependent but linked processes will most likely be two pieces of contradictory guidance.	published in Jan 2020). The committee considered carefully the results from the additional analysis and decided to make a minor change in section 1.3 to reflect uncertainties in the cost saving of using Rezum or UroLift by removing the comparative costs of 2 minimal invasive procedures and including a statement noting uncertainties in the cost saving when Rezum is compared with UroLift.
37	6	manufacturer (other)	These improvements were sustained throughout 4 years of follow up	Statements regarding certainty of durability of effect should be carefully scrutinised. In its appraisal of the Rezum II study [MT413 Rezum Supporting documentation], the EAC stated that "the prospective case series, derived from the patients receiving the intervention, was subject to considerably more potential for bias. As patients were unmasked, there was a potential for detection bias, especially since most outcomes were subjective (Higgins and Green, 2015). Analysis of the single-armed data was performed per protocol (PP) and attrition rates were significant, with 34% of patients not providing outcome data at 4 years (McVary et al., 2019). There was also a potential for reporting bias, and there does not appear to	Thank you for your comment. The committee considered your comment carefully and acknowledged that the limitations of included studies reported in the assessment report (see section 5.2). The EAC advised that treatment response may be diminishing when aging is taken into account. A similar effect is seen with UroLift; a graphical comparison is made in Figure 7.1 of the assessment report. In both cases, there is statistical improvement in IPSSS compared with baseline throughout the study follow-ups.

				have been any attempt to account for multiple comparisons when significance levels were reported." In addition, according to McVary et al 2019 (Rezum II study); the results obtained in mean IPSS improvement from baseline were “early response at 3 months (49.9%) to years 1 (52.2%), 2 (50.7%), 3 (49.7%) and 4 (46.7%)”. These results are suggestive of a decreasing response beyond year 1 rather than a sustained improvement throughout 4 years as stated.	The committee decided not to change the guidance.
38	6	Manufacturer (other)	These improvements were gained without significantly adversely affecting sexual function	This is a misleading statement based on the evidence and may mislead patients into making choices about treatment based on an understanding that that their sexual function will be preserved. All thermal ablation procedures, including steam, have shown collateral damage of the prostate that leads to sporadic loss of ejaculatory function. MTG529 does not consider this important side effect and in fact assumes it to be the same as UroLift, which is the only treatment for BPH to never have a patient to have lost ejaculatory function in any report. The Rezum data is similar to the prior thermal ablation procedures because the mechanism of action is the same. Collateral damage to the bladder neck, ejaculatory ducts, and/or tissue surrounding the veru montanum are all potential causes of inconsistent results. The Rezum II study report avoids stating that Rezum preserves ejaculatory function because it does not reliably do so. While mean MSHQ-EjD scores were stable and even showed some improvement, 2.9% patients completely lost function (anejaculation) and 2.9% experienced “reduced ejaculatory volume”. This is similar to the 3.1% anejaculation reported by Mollengarden et al in the real world study of Rezum (Prostate Cancer Prostatic Dis. 2018 Sep;21(3):379-385). It is inappropriate to report adverse events simply as mean scores, since this hides low rates. If incontinence were treated this way, we would not acknowledge the possibility for incontinence after HoLEP or TURP, since mean scores stay largely level. This collateral damage associated with thermal ablation	Thank you for your comment. Please see the response to comment 34.

				can be increased with more aggressive ablation, as seen in a report from the Mayo Clinic. Yang et a,l from the Mayo Clinic, reported 20% anejaculation after Rezum; this was presented at conference [Yang DY et al. Abstract presented at AUA conference. 2018. Poster UP3-33 Prevalence of Ejaculatory Dysfunction Following Rezum Prostate Ablation] and is described in a comparison of Rezum and UroLift [Kaplan SA. Demistifying less-invasive solutions for BPH. Urology Times. Sept 2019]. Ines et al conducted a more in-depth report of sexual dysfunction after Rezum, showing 17% anejaculation [Ines M et al. A retrospective review of the Rezum System: Treatment for benign prostatic hyperplasia in men with mild, moderate and severe lower urinary tract symptoms. NSAUA Sept 2019]. Many NHS patients elect to have UroLift treatment instead of more invasive treatments in order to preserve sexual function. To not warn these men that Rezum does not offer the same certainty is a disservice to patients in whom these outcomes are important.	
39	6	Manufacturer (other)	people were less likely to need further operations after Rezum than after UroLift. The retreatment rate was 4.4% at year 4 with Rezum and 13.6% at year 5 with UroLift.	Statements comparing the efficacy of Rezum with Urolift should be carefully scrutinised and removed if they cannot be fully supported by the evidence. Conclusions comparing clinical outcomes between Urolift and Rezum based on results of Rezum II study and the LIFT study are inherently biased in favour of Rezum, due to the fact that the study populations were different in the following critical aspects: • The LIFT study excluded treatment of obstructing middle lobe (OML). McVary et al (Rezum II study) demonstrated that treatment of OML enhanced the overall IPSS and Qmax effect seen in this study. In a recently published study with Urolift, looking at use in patients with OML (MedLIFT study), Rukstalis et al showed that treatment of OML shows a significantly greater effect on both IPSS (13.5 vs 10.6) and Qmax (6.4 vs 4.0 ml/s) [Rukstalis D et al. Prostate Cancer and Prostatic Diseases 2019;22: 411-419] • What is significant about this is that MedLift was an FDA IDE extension of the L.I.F.T. randomised study, designed to examine safety and efficacy of Urolift for treatment of	Thank you for your comment. The committee considered your comment carefully and was aware of the lack of evidence for a direct comparison between Rezum and UroLift. The committee understood that the Rezum II trial and LIFT trials were very similar in terms of study design and the baseline characteristics of study population., The committee was aware that the LIFT trial excluded patients with obstructing middle lobe involvement, and that 37% of patients with this condition were included in the Rezum II study. The committee was also aware of the new evidence demonstrating that UroLift can now be used to treat median lobe obstruction. Please see the response to comment 35. The committee is aware that the LIFT study reported that 26% of patients were in partial retention and the Rezum study

				obstructive middle lobes (OML). Inclusion criteria were identical to the LIFT study, except for requiring an OML. The MedLIFT study was not included for consideration in the current MTEP evaluation of Rezum when comparing Rezum with Urolift, which introduces the potential for clinical bias towards Rezum when comparing these two treatments in men with OML. • Rukstalis et al went further in analysis to compute what the overall changes were in LIFT/MedLIFT if middle lobe was included. The result (11.4 IPSS, 4.7ml/s Qmax) supports the lack of any significant chronic difference in effect between UroLift and Rezum. The Rezum II patient inclusion with regard to Qmax also biased results in favour of Rezum, when making outcome comparisons to the LIFT study. The Rezum II study excluded any patient with a baseline Qmax of less than 5 ml/s, whereas the LIFT study had no lower limit except complete retention. In LIFT, 26% patients were in this category of "near retention", a patient population that, on average, has been shown to be less likely to have a quantitative improvement in Qmax [Guo DP et al. Int J Urol 2017;24:703-707].	excluded patients with urinary retention. As the evidence on the efficacy of using Rezum for people with urinary retention is sparse, the committee agreed to future research to evaluate the use of Rezum in this group of the population would be valuable (see section 4.15).
40	6	Manufacturer (other)		Statements comparing the durability of Rezum with Urolift should be carefully scrutinised and removed if they cannot be fully supported by the evidence. The EAC noted there was "uncertainty" in the reported retreatment rates of 4.4% at year 4 due to substantial patient attrition. As noted by the EAC in its report [MT413 Rezum Supporting documentation], "analysis of the single-armed data was performed per protocol (PP) and attrition rates were significant, with 34% of patients not providing outcome data at 4 years (McVary et al., 2019)." The LIFT study, on the other hand showed 13.6% retreatment rate for Urolift at both 4 and 5 years with only 9% patients missing. Real world NHS experience with Urolift have shown considerably lower retreatment rates. We would ask the Committee to consider that there is	Thank you for your comment. The committee considered your comment carefully. It was aware of the differences in the retreatment rates in the studies. The EAC advised that there was no evidence that the rates were underestimated for Rezum or overestimated for Urolift. Clinical experts noted that the differing mechanisms of action may explain the tendency of low retreatment rate using Rezum compared with UroLift. The committee decided not to change the guidance.

				enough unknown in the Rezum study to cast a doubt on a conclusive difference between Rezum and Urolift in this regard. Common sense would also suggest that a 1.1% retreatment per year reported for Rezum is lower than that reported in most studies of TURP, HoLEP, and Greenlight. There is no clinical reason to expect a lower retreatment from a procedure that similarly reduces tissue but to a much lesser extent than these surgeries.	
41	6	Manufacturer (other)	The committee noted that there are no studies that directly compare Rezum with other treatments in relieving symptoms in people with BPH, but considered an indirect comparison between Rezum and UroLift, that was drawn from analogous trial data. This suggests that Rezum is at least as effective as UroLift over 4 years	It should be noted that the main comparator for Rezum is TURP, which remains the current standard of care in the NHS. Persistent comparison of Rezum with Urolift throughout this review is not based on any direct comparative studies and comparisons made are based on comparing data from separate studies that are not analogous as stated in statement 4.1. Statements comparing the efficacy of Rezum with Urolift should be carefully scrutinised and removed if they cannot be fully supported by the evidence. Conclusions comparing clinical outcomes between Urolift and Rezum based on results of Rezum II study and the LIFT study are inherently biased in favour of Rezum, due to the fact that the study populations were different in the following critical aspects: • The LIFT study excluded treatment of obstructing middle lobe (OML). McVary et al (Rezum II study) demonstrated that treatment of OML enhanced the overall IPSS and Qmax effect seen in this study. In a recently published study with Urolift, looking at use in patients with OML (MedLIFT study), Rukstalis et al showed that treatment of OML shows a significantly greater effect on both IPSS (13.5 vs 10.6) and Qmax (6.4 vs 4.0 ml/s) [Rukstalis D et al. Prostate Cancer and Prostatic Diseases 2019;22: 411-419]. What is significant about this is that MedLift was an FDA IDE extension of the L.I.F.T. randomised study, designed to examine safety and efficacy of Urolift for treatment of obstructive middle lobes (OML). Inclusion criteria were identical to the LIFT study, except for requiring an OML. The MedLIFT study was not included for consideration in the current MTEP evaluation of Rezum when comparing Rezum with Urolift, which introduces the	Thank you for your comment. The committee considered your comment carefully and acknowledged that the lack of direct comparison of Rezum with other technologies. Nevertheless, the committee understood that the Rezum II and LIFT trials were sufficiently similar, and the indirect comparison was useful to inform the committee's decision making. Please also see the response to comment 39.

				potential for clinical bias towards Rezum when comparing these two treatments in men with OML. • Rukstalis et al went further in analysis to compute what the overall changes were in LIFT/MedLIFT if middle lobe was included. The result (11.4 IPSS, 4.7ml/s Qmax) supports the lack of any significant chronic difference in effect between UroLift and Rezum. • The Rezum II patient inclusion with regard to Qmax also biased results in favour of Rezum, when making outcome comparisons to the LIFT study. The Rezum II study excluded any patient with a baseline Qmax of less than 5 ml/s, whereas the LIFT study had no lower limit except complete retention. In LIFT, 26% patients were in this category of "near retention", a patient population that, on average, has been shown to be less likely to have a quantitative improvement in Qmax [Guo DP et al. Int J Urol 2017;24:703-707].	
42	6	Manufacturer (other)	Section 4.3: Overall, the committee concluded that sexual function is preserved with Rezum, at least in the short term	This is a misleading statement based on the evidence and may mislead patients into making choices about treatment based on an understanding that that their sexual function will be preserved. All thermal ablation procedures, including steam, have shown collateral damage of the prostate that leads to sporadic loss of ejaculatory function. MTG529 does not consider this important side effect and in fact assumes it to be the same as UroLift, which is the only treatment for BPH to never have a patient to have lost ejaculatory function in any report. The Rezum data is similar to the prior thermal ablation procedures because the mechanism of action is the same. Collateral damage to the bladder neck, ejaculatory ducts, and/or tissue surrounding the veru montanum are all potential causes of inconsistent results. The Rezum II study report avoids stating that Rezum preserves ejaculatory function because it does not reliably do so. While mean MSHQ-EjD scores were stable and even showed some improvement, 2.9% patients completely lost function (anejaculation) and 2.9%	This is a duplicate. Please see the response to comment 38.

				experienced “reduced ejaculatory volume”. This is similar to the 3.1% anejaculation reported by Mollengarden et al in the real world study of Rezum (Prostate Cancer Prostatic Dis. 2018 Sep;21(3):379-385). It is inappropriate to report adverse events simply as mean scores, since this hides low rates. If incontinence were treated this way, we would not acknowledge the possibility for incontinence after HoLEP or TURP, since mean scores stay largely level. This collateral damage associated with thermal ablation can be increased with more aggressive ablation, as seen in a report from the Mayo Clinic. Yang et a,l from the Mayo Clinic, reported 20% anejaculation after Rezum; this was presented at conference [Yang DY et al. Abstract presented at AUA conference. 2018. Poster UP3-33 Prevalence of Ejaculatory Dysfunction Following Rezum Prostate Ablation] and is described in a comparison of Rezum and UroLift [Kaplan SA. Demistifying less-invasive solutions for BPH. Urology Times. Sept 2019]. Ines et al conducted a more in-depth report of sexual dysfunction after Rezum, showing 17% anejaculation [Ines M et al. A retrospective review of the Rezum System: Treatment for benign prostatic hyperplasia in men with mild, moderate and severe lower urinary tract symptoms. NSAUA Sept 2019]. Many NHS patients elect to have UroLift treatment instead of more invasive treatments in order to preserve sexual function. To not warn these men that Rezum does not offer the same certainty is a disservice to patients in whom these outcomes are important.	
43	6	Manufacturer (other)		Statements regarding certainty of durability of effect should be carefully scrutinised. In its appraisal of the Rezum II study [MT413 Rezum Supporting documentation], the EAC stated that “the prospective case series, derived from the patients receiving the intervention, was subject to considerably more potential for bias. As patients were unmasked, there was a potential for detection bias, especially since most outcomes were subjective (Higgins and Green, 2015). Analysis of the single-armed data was performed per protocol (PP) and attrition rates were significant, with 34% of patients not providing outcome data at 4 years (McVary et al., 2019). There was also a	This is a duplicate. Please see the response to comment 37.

				potential for reporting bias, and there does not appear to have been any attempt to account for multiple comparisons when significance levels were reported."	
44	6	Manufacturer (other)	The committee concluded that the evidence is generalisable to UK NHS practice.	The recommendations, based on studies performed outside of the UK, that Rezum can be done under a local anaesthetic or light sedation does not reflect actual NHS practice. In the results of a Patient Questionnaire, provided in the MT413 Rezum Supporting documentation – Committee papers, 75% of patients had a general anaesthetic. In the Adoption Scoping Report, also in the Supporting Documentation, the 9 Urologists who were consulted (7 of which use Rezum) said the method of anaesthesia was general anaesthetic, sedation with local anaesthetic or spinal block. Almost all patients who undergo treatment with Rezum are catheterised; reportedly from the studies (outside the UK) for an average of 3-4 days, although the responses to the 30-NHS patient Rezum patient questionnaires in the MT413 Rezum Supporting documentation, suggests a much longer duration of catheterisation of 1-2 weeks.	Thank you for your comments. Please see the response to comment 3 regarding the types of anaesthetics. The committee considered your comment about the catheter and agreed that everyone undergoing Rezum need catheterisation. The clinical experts note that the length of catheterisation is typically 5 to 7 days but this varies depending on individual factors such as co-morbidities. The committee decided to make a minor change in the guidance (see section 4.5) to note the advice received about the length of catheterisation after Rezum in clinical practice.
45	7	NHS professional	Rezum is more versatile than UroLift in treating different shapes of prostate, for example in men with an obstructive median lobe.	There is no restriction on median/middle lobe treatment with Urolift. The MEDLIFT study showed good results with middle lobe treatment, so it would be misleading to suggest Rezum is more versatile. You could argue that Urolift is more versatile as prospective retention data presented at AUA 2019 shows good result for Urolift, and no such data exists for Rezum.	Thank you for your comment. Please see the response to comment 35.
46	7	NHS professional	There is no evidence that directly compares Rezum with other interventions for BPH	I think it would be helpful to compare Urolift with Rezum if there were any available prospective data available to look at this. There is scope for a trial here. Patients who we counsel about all these options often want to know about the perioperative experience with both, as the IPSS and flow rate improvements are very similar. It is the perioperative and early post-operative experience which differs and this is how they will decide. At present we have only expert opinion to describe this. In my experience of both these treatments, Rezum patients need a catheter for 5-7 days (up to a month if in retention) and have a	Thank you for your comment and sharing your clinical experience. The committee was aware of the lack of evidence and consider further research to compare Rezum with other surgical treatments would be valuable (see section 4.15). Please also see the response to comment 44 about the use of a catheter after Rezum.

				relatively stormy time with visits to GP/nurse/ED/telephones to hospital, which is not readily described in existing literature. Having said this, when we review at three months, they will say that, although they had a bumpy ride, it was worth it in the end. Patients need to be aware of this and it should be studied with PROMs ideally to help to inform their choice.	
47	7	NHS professional	An indirect comparison suggests that Rezum is as effective as UroLift	The retreatment rate of 4.4% for Rezum is low, but a large number of men in this trial were lost to follow up, and this may skew the rate. If compared to a larger series of Urolift patients (real world data study published Sep 2019), the retreatment rate for PUL was 5% and in my series with up to 5 years follow up it is 7%. The slightly higher rate from the LIFT study may be due to the fact that these were surgeons in the early phase of their learning , who had only done 6-7 cases each. This is not reflective of current practice and should not be used exclusively as the only quoted retreatment rate, as it is likely an overestimate of current practice.	Thank you for your comment. The committee considered your comment carefully. Advice from the clinical experts was that the retreatment rate for Rezum in clinical practice is probably about1% higher than that reported in the pivotal study. The committee is aware that there is no real-world data on retreatment rates available to compare the difference reported in the published studies and clinical practice. The committee decided not to change the guidance
48	8	NHS professional	The clinical experts confirmed that, in their clinical practice, this cohort of patients corresponds closely to those that they treat with Rezum and that this encompasses approximately 75% to 85% of the overall population that need treatment to relieve LUTS.	In Rezum II 387 men with LUTS were initially investigated for the trial but only 197 (51%) met the inclusion criteria - it may not therefore be truly generalisable to NHS practice	Thank you for your comment. The committee considered your comment carefully and acknowledged over half of initially investigated patients were included in the Rezum II study. The reasons for exclusion of the 187/384 (49%) in Rezum II were not reported in the study, but there were 35 exclusion criteria detailed in the protocol (NCT01912339). The committee however did not consider this pertains to generalisability to the NHS, because people who experience LUTS and are eligible for treatment are similar in the NHS compared with those in the US. The committee decided not to change the guidance
49	8	NHS profession	the company did an indirect comparison of Rezum and UroLift	This is very poor quality of information on which to make a major decision that could result in major changes in NHS practice.	Thank you for your comment. The committee acknowledged the limitations of evidence in terms of quantity and quality available on Rezum and agreed more evidence will improve the

					evidence base on the efficacy of Rezum compared with other technologies for treating LUTS due to BPH (see section 4.15).
50	8	NHS professional	They pointed out, however, that Rezum is more versatile than UroLift in treating different shapes of prostate, for example in men with an obstructive median lobe.	This flies in the face of the latest NICE guidance: Review of MTG26: UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia (Jan 2020) Based on the paper by Rustalis et al. (2018) evidence shows that Urolift can also be done in patients with median lobes with good symptomatic and flow rate improvements. This guidance finishes with the statement below suggesting the indications for Rezum and Urolift are equivalent: The Rezum procedure involves water vapour therapy and has a similar indication to the UroLift system: for treating lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) in those aged 50 or over, and with prostate volumes no greater than 100 cc (100 g). Suggesting that the patient populations are the same	Thank you for your comment. Please see the response to comment 35.
51	8	NHS professional	Nonetheless, the clinical experts explained that the study population included in the Rezum II study is similar to the people that they treat with Rezum in their own practice in the NHS.	Nonetheless half the patients who presented for entry to the Rezum II study did not meet the inclusion requirements - this may not therefore be generalisable into NHS Practice	Thank you for your comment. Please see the response to comment 48.
Cost modelling (n=21)					
52	1	NHS professional (commissioner)	Consultation question	*Are the summaries of clinical and resource savings reasonable interpretations of the evidence?* Clinical yes but resource savings has not been accurately reflected as they only consider provider costs and not the costs incurred for the intervention ie. Payment by Results charges.	Thank you for your comment. Please see the response to comment 6.
53	2	NHS professional	Consultation question	*Are the summaries of clinical and resource savings reasonable interpretations of the evidence?*	Thank you for your comment. The committee agreed that one of the key gaps in the evidence is that there was no direct evidence identified comparing

				The assumption that all laser TURP patients are discharged the same day is unlikely to be correct and needs verifying with HES data.	Rezum with any of its comparators. The clinical experts advised that invasive procedures such as TURP are likely to result in better improvement in LUTS relief compared with Rezum. The committee understood this was a limitation of the cost modelling. as noted in section 4.11. It agreed that future research comparing Rezum with other surgical treatments would be welcome (see section 4.15).
54	4	NHS professional	Consultation question	*Are the summaries of clinical and resource savings reasonable interpretations of the evidence?* Agree	Thank you for your comment.
55	5	Lay person	Consultation question	*Are the summaries of clinical and resource savings reasonable interpretations of the evidence?* I have made no comments on clinical or resource savings.	Thank you for your comment.
56	8	NHS professional	Consultation question	*Are the summaries of clinical and resource savings reasonable interpretations of the evidence?* No - see comments below.	Thank you for your comment.
57	9	NHS professional	Consultation question	*Are the summaries of clinical and resource savings reasonable interpretations of the evidence?* Please see my comments below. Should try to incorporate.	Thank you for your comment.
58	1	NHS professional (commissioner)	Cost modelling overview	This section needs further consideration in light of previous comments associated with the actual cost to the NHS of these interventions as opposed to the costs incurred by providers.	Thank you for your comment. Please see the response to comment 6.
59	1	NHS professional (commissioner)	Cost saving	May be influenced by re-worked costings	Thank you for your comment.
60	6	Manufacturer (other)	Rezum is cost saving compared with: UroLift by £497	This cost comparison uses inaccurate assumptions for Urolift and does not fully cost the pathway for Rezum. This comment is expanded later in comments on the relevant sections	Thank you for your comment. The committee considered your comment carefully and was aware that MTG26 was used as one of data sources for UroLift related costs when compared with Rezum. Experts were also consulted about the assumptions for the use of UroLift in clinical practice. The EAC ran an additional analysis varying clinical parameters in the cost modelling when Rezum is compared with UroLift, and results suggested uncertainties of the cost

					saving between 2 technologies. The committee discussed the results and decided to make change the recommendation 1.3 to reflect uncertainties in the cost saving of using Rezum or UroLift by removing the comparative costs of 2 minimal invasive procedures and including a statement noting uncertainties in the cost saving when Rezum is compared with UroLift. Please also see the response to comments 63.
61	6	Manufacturer (other)	Rationale: Rezum is also cost saving compared with UroLift because of low consumable costs.	This is a misleading statement. The consumable costs for Rezum are not “low” in comparison to TURP and laser treatments, and only slightly lower than Urolift, which in the economic base case wrongly assumes 4.4 implants. This assumption of 4.4 Urolift implants is incorrect and should be changed in the base case to 4 implants, which accurately reflects the assumptions that were used in the final base case of MTG26. Correcting this assumption brings the consumable cost for Rezum and Urolift within £68 of one another; a cost differential that is more than removed by correcting the length of stay (LOS) for Urolift to again reflect the LOS used in the final base case of MTG26. This is expanded in a later comment.	Thank you for your comment. The committee considered your comment carefully, and understood that the number of UroLift (4.4 implants) was sourced from the MTG26. The EAC ran additional analysis for the cost comparison between Rezum and UroLift by varying parameters including changing the number of UroLift implants to 4 (see table 1 and table 2 in appendix 1). The results showed Rezum remains cost saving compared with UroLift when individual parameters are varied. However, when all the parameters are combined the base case becomes cost incurring and the probabilistic sensitivity analysis results indicate that there is uncertainty about the cost savings (section 3.9). The committee discussed the results and agreed that the cost saving of Rezum compared with UroLift is subject to uncertainty, and decided to amend the recommendation 1.3 to reflect uncertainties in the cost saving of using Rezum or UroLift by removing the comparative costs of 2 minimal invasive procedures and including a statement noting uncertainties in the cost saving when Rezum is compared with UroLift.

62	6	Manufacturer (other)		The economic modelling, both that of the sponsor and subsequently by the EAC, which informs the recommendations around cost comparison of Rezum and Urolift, use erroneous cost assumptions, which are unsupported in evidence and, where Urolift is concerned, directly contradict the NICE MTG for Urolift (MTG 26, 2015). Details of these errors are provided in later comments. In addition, the economic modelling does not take into account the full treatment pathway for Rezum and the other comparators as regards follow-up visits to hospital and visits to hospital to have the catheter removed. These are important factors when comparing Rezum with Urolift, where, in the case of Urolift treatment, patients are followed up by telephone and are not routinely catheterised, so there is no requirement for a hospital visit to have the catheter removed.	Thank you for your comment. The committee considered your comment carefully, and acknowledged that all assumptions for the cost modelling are based on published sources and/or expert opinions if there is no published data. In the initial cost modelling, the cost of catheter removal was not included for Rezum and other comparators. In the EAC's additional analysis, the cost of catheter removal is included when compared Rezum with UroLift, and the result show Rezum is cost saving by £351 per patient over 4 years (see table 2 in appendix 1). Please see response to comment 60.
63	6	Manufacturer (other)		Some of the assumptions in the model with regard to Urolift do not accurately reflect the evidence or the current NICE guidance (MTG26) and therefore the cost comparison conclusions regarding the cost difference between Rezum and Urolift are incorrect and bias in favour of Rezum. • TECHNOLOGY COSTS. Number of Urolift implants. The economic model erroneously uses 4.4 Urolift implants per treatment. The correct number of implants should be 4. This is the number of implants used in the NICE guidance for Urolift (MTG26 Costing Statement https://www.nice.org.uk/guidance/mtg26/resources/costing-statement-pdf-487330957) and is supported by >5 years of NHS clinical practice. By changing this to 4 implants instead of 4.4, the differential in consumables cost between Urolift and Rezum is reduced from £189 to <£50. • HOSPITAL LENGTH OF STAY. The economic model erroneously uses a length of stay of 0.5 days for Urolift. The correct length of stay for Urolift is 0.125 days, which was the length of stay agreed and used on the final base case for the Urolift NICE guidance (MTG26; pages 11 and 92 https://www.nice.org.uk/guidance/mtg26/documents/urolift-	Thank you for your comment. The committee considered your comment carefully, and these issues are addressed individually below. Please also see the response to comment 61. <u>Technology costs</u> The EAC ran an additional analysis using the assumption of 4 implants (see table 1 in appendix 1). Rezum remains cost saving by £353 per patient over 4 years in this scenario. <u>Hospital length of stay</u> The EAC ran additional analysis using the assumption of the shorter length of stay for UroLift. Rezum remains cost saving by £356 per patient in this scenario (see table 1 in appendix 1). <u>Theatre time</u> The EAC's additional analysis indicated that Rezum would remain cost saving by £325 when the procedure time was 20 minutes (see table 1 in appendix 1).

				for-treating-lower-urinary-tract-symptoms-of-benign-prostatic-hyperplasia-assessment-report2). This length of stay (routinely 3 hours) has been confirmed in numerous reports from NHS hospitals and is confirmed in the last 2 years of HES data. By using 0.5 days length of stay for Urolift, this is inaccurate and further biases the cost comparison in favour of Rezum • THEATRE TIME. The theatre time used in the economic modelling for Rezum (17.5 minutes) is at the lower end of the estimates (17 to 25 minutes) reported by NHS clinicians in the EAC report. There is no strong literature published to base this on and using a lower estimate of theatre time biases this parameter of the cost in favour of Rezum when compared with Urolift. There should be parity in the theatre time used with Rezum and Urolift. The theatre time for Urolift, which is supported by NHS clinical opinion and reflected in reports of Urolift experience presented at conference is 10-30 mins; 10 mins reported by Leeds NHS Trust [Poster presented at WCE 2018. Young M. Transforming BPH surgical care to an ambulatory setting - what are the gains and losses?], 25 mins reported by Norfolk and Norwich University Hospital, based experience with 250 patients [https://www.nice.org.uk/sharedlearning/adoption-of-urolift-procedure-an-ambulatory-pathway-for-patients-suffering-from-lower-urinary-tract-symptoms-of-benign-prostatic-hyperplasia], 20 mins reported by Northampton General Hospital [poster presented at BAUS 2019. Carrie A and Nemade H. Comparative cost effectiveness of Urolift procedure vs TURP.] and 20-30 mins reported by Royal Devon & Exeter [https://www.nice.org.uk/sharedlearning/urolift-a-community-based-alternative-treatment-for-benign-prostatic-obstruction-bpo]. Importantly, two contributors to the Rezum Adoption Scoping Report [MT413 Rezum Supporting documentation, Page 2 of 11] said they dedicate 25-30 minutes per case (not including anaesthetic induction and anaesthetic recovery) and all contributors agreed that between 5 and 6 cases could be done in a single theatre session. In this time, contributors thought a	<u>Routine post procedure hospital visits</u> The committee understood that nearly all Rezum patients require a hospital appointment to remove catheter. The EAC ran an additional analysis to include the cost of catheter removal in the model when Rezum was compared with UroLift. The result suggested that Rezum would remain cost saving by £351 when this cost was included (see table 1 in appendix 1). <u>Adverse events</u> The committee acknowledge that these adverse events were captured in the cost model, and were informed by the best empirical data available.). The committee understood that the AE rate for Rezum is relatively low, especially for serious AEs, they have little impact on the model. <u>Retreatments</u> The committee acknowledged that the model incorporated the best-long term data available on the need for retreatment in patients receiving Rezum or UroLift. Retreatment was a fundamental part of the model submitted by the company and retreatment rates were taken from 2 trials of almost exactly the same design (Rezum II and LIFT). These are the best data available despite the high attrition rate (which applies to both studies). Clinical experts advised that it was mechanistically plausible that UroLift would inevitably result in a higher retreatment rate (as it does not ablate tissue for the Rezum procedure). There are limitations that cause substantial uncertainty in the Rezum II trial but these equally apply to the LIFT

				similar number of Urolift procedures, 2 to 4 TURP procedures or 2 HoLEP procedures can be done. By using a significantly lower theatre time (nearly 50% lower), the modelling biases the costs in favour Rezum vs Urolift to an amount of £167. • ROUTINE POST PROCEDURE HOSPITAL VISITS. Post procedure hospital visits that are routinely part of the treatment pathway for Rezum were not included in the economic modelling. This unfairly introduces bias against Urolift, which, unlike all the other treatments compared in this MTG, does not require any routine post procedure follow-up visits. o HOSPITAL VISIT TO REMOVE CATHETER. In its report the EAC acknowledged that Rezum patients are typically discharged with a catheter in situ, and require an outpatient appointment to have this removed. However, the EAC stated that this cost was not captured by the model, but said that post-discharge costs for other modalities were also not accounted for. However this introduces bias in the model in against Urolift, where patients are not routinely catheterised and therefore, unlike Rezum, do not require the extra outpatient appointment to have the catheter removed. The EAC argues that these costs are not easily quantified and adds this is a limitation of the model that adds some uncertainty to the results. We would like the Committee to consider that the availability of NHS National Reference costs enables an easy way to quantify an outpatient appointment to remove a urinary catheter: Procedure code OPCS M47.3 Removal of urethral catheter from bladder. Maps to HRG LB15E. National Reference cost (2017/18) – Outpatient procedure (OPROC): £144 o FOLLOW-UP HOSPITAL VISIT. Rezum, TURP and laser treatments all routinely require a follow-up consultant-led outpatient appointment. Urolift patients, on the other hand, are routinely followed up by a nurse on the telephone. To not include the cost of these routine hospital visits in the economic modelling is to introduce unfair bias against	trial. Clinical experts agreed that because Rezum ablates prostatic tissue but UroLift does not, it is likely to have greater permanence. The EAC updated the data on the proportion on the modality of retreatment to align with the data reported in the LIFT trial. It may be true that a repeat UroLift requires less implants than a first procedure, but this is not evidenced. It is not possible to introduce this into the model without substantially changing the model structure and it would make very little difference to the final aggregated costs.

				Urolift. Again, National Reference costs can be used to quantify this cost: Consultant-led follow-up outpatient visit: National Reference cost (2017/18). Service code 101 Urology: £112. For comparison in the model, routine follow-up for Urolift is by telephone. An estimate of cost, based on 10 mins of nurse time (Band 6) and call charges is £20 [Unit cost source: PSSRU 2019]. • ADVERSE EVENTS. As our comment on Section 3.5, significant adverse effects of Rezum appear to have been overlooked and this lends bias when considering Rezum and UroLift are being compared as similar “minimally invasive” treatments. This MTG excludes consideration of important evidence distinguishing these therapies from each other: a) post-operative urinary retention, requirement for catheterisation, catheter-associated complications, UTI and urosepsis; and b) sexual dysfunction. It is critical that these adverse events are properly costed in order to avoid cost bias in favour of Rezum over Urolift, which is associated with a significantly lower incidence of AEs, particularly CAUTIs, retention and impact on sexual function. • RETREATMENTS. The assumptions used in the retreatment parameter of the economic modelling result in a significant cost difference between Rezum and Urolift (£97 vs £257). And yet The EAC noted there was “uncertainty” in the reported retreatment rates of 4.4% at year 4 due to substantial patient attrition. As noted by the EAC in its report [MT413 Rezum Supporting documentation], “analysis of the single-armed data was performed per protocol (PP) and attrition rates were significant, with 34% of patients not providing outcome data at 4 years (McVary et al., 2019).” The Committee also heard from clinical experts (Committee Discussion section 4.6) who suggested that the average retreatment rate in their experience is around 3% after Rezum, and that retreatment is most likely in the first year after the procedure. We would ask the Committee to consider if there is enough unknown in the Rezum study to cast a doubt on a conclusive difference between Rezum and	

				Urolift in this regard, particularly when it impacts on the economic comparisons so greatly. In terms of Urolift, the base case in the economic modelling assumes that in Urolift patients who require retreatment, 63% received TURP and 37% receive repeat UroLift. However, it needs to consider that when there is a retreatment with UroLift, it is performed most of the time with one implant (maximum 2) and is therefore associated with less consumable costs compared with the initial treatment. Also real-world NHS experience with Urolift have shown considerably lower retreatment rates than those reported in the LIFT study.	
64	6	Manufacturer (other)		After correcting for the erroneous assumptions detailed in our comments on section 3.7 and also after adding in the full pathway costs of routine post-op hospital visits (also detailed in our comments on section 3.7), we dispute that Rezum is cost saving compared with Urolift.	Thank you for your comment. The committee considered your comment carefully, and acknowledged that all assumptions for the cost modelling are based on published sources and/or expert opinions if there is no published data. The EAC ran additional analysis to reflect clinical practice using the technologies, and the committee agreed that the direction of cost saving between Rezum and UroLift is not uncertain, and agreed to make a minor change to the recommendation 1.3 to reflect uncertainties in the cost saving of using Rezum or UroLift by removing the comparative costs of 2 minimal invasive procedures and including a statement noting uncertainties in the cost saving when Rezum is compared with UroLift.
65	6	Manufacturer (other)		This would appear to be contradicted by HES data from NHS trusts, where length of stay for GreenLight can be identified because the trust exclusively performs GreenLight laser (and not HoLEP). Routinely, length of stay is 1 day or more.	Thank you for your comment. The committee considered your comment carefully, and acknowledged the potential uncertainty in the length of stay after GreenLight (see the assessment report section 9.2, page 69). The committee decided not to change the guidance.
66	7	NHS professional	Rationale: Rezum is also cost saving compared with UroLift because of	In my series of around 300 Urolifts, the average implants per patient is 3.1 not 4.4 implants which was used in the modelling. So consumable cost is similar, but	Thank you for your comment and sharing your experience using UroLift implants. the EAC ran an additional analysis using the assumption of 4 implants. Rezum

			low consumable costs.	UTI/reattendance is higher with Rezum, which is not included in the calculation.	remains cost saving by £353 per patient in this scenario (see table 2 in appendix 1).
67	7	NHS professional		The cost of postoperative UTI/healthcare contact with Rezum probably is underestimated in the calculations in this document.	Thank you for your comment. Please see the response to comment 63 relating to adverse events.
68	7	NHS professional		The average number of Urolift implants in my practice is 3.1 not 4.4 used in this economic modelling. Length of stay in my practice for Urolift is 3 hours not 0.5 days used in this modelling Theatre time for cases - We would do 5 Rezum cases in a 4 hour session, about 30 min each case. For Urolift we allocate 20-25 min (but have more experience of this). I would say theatre time is comparable between Urolift and Rezum. Catheter is always placed after Rezum, and the health system incurs a cost for this. Some men (perhaps 1;4) fail the first TWOC and need a second TWOC. There is morbidity associated with catheterisation for 7-14 days. For Urolift, standard of care is not to use a catheter and they will be needed perhaps 1:20 cases if haematuria in larger prostates for 12-24h.	Thank you for your comment and sharing your clinical experience with us. Please see the response to comment 63.
69	7	NHS professional		I don't think it is reasonable to say Rezum is cost saving compared to Urolift. These two treatments are comparable in that regard in my experience.	Thank you for your comment. The committee considered the comment and the cost modelling. The EAC ran an additional analysis to reflect clinical practice using UroLift, and the committee agreed that the direction of cost saving between Rezum and UroLift is not uncertain, and agreed to make a change to the recommendation 1.3 to reflect uncertainties in the cost saving of using Rezum or UroLift by removing the comparative costs of 2 minimal invasive procedures and including a statement noting uncertainties in the cost saving when Rezum is compared with UroLift.

70	8	NHS professional	Cost evidence	Comparison with other minimally invasive procedures, with regard to economic comparisons is subject to bias without RCTs of a high quality.	Thank you for your comment.
71	8	NHS professional	The company developed a decision analytic model with a time horizon of 4 years. The model compared Rezum with 4 comparators: UroLift, GreenLight laser, HoLEP and TURP. The model assumed that all the technologies had equal efficacy in alleviating LUTS associated with BPH	These modalities do not have equivalent effects on efficacy. This is a flawed assumption. Urolift is a direct comparator to Rezum but TURP , HoLEP and G-L laser have superior outcomes symptomatically and objectively with flow rate, prostate volume reduction and residual volume reductions	Thank you for your comment. Please see the response to comment 53.
72	8	NHS professional	The EAC's changes to the cost model more accurately reflect empirical evidence and expert opinion	Did this include the return visit for a trial without catheter and voiding monitoring after approx 4 days that the majority of patients require and the 14% subsequent retention requiring repeat catheterisation?	Thank you for your comment. The committee considered your comment carefully, and acknowledged the cost of catheter removal was not included in the cost model. Please see the response to comment 44 and the clinical experts noted that all patients have a hospital appointment for removing catheter. The EAC ran an additional analysis to include this cost, and the result shows that Rezum remain cost saving by £351 per patient compared with UroLift in this scenario (see table 2 in appendix 1). The committee was also aware that none of studies reported the rate of subsequent retention after Rezum..
Side effects (n=12)					
73	6	Manufacturer (other)		Significant adverse effects of Rezum appear to have been overlooked and this lends bias when considering Rezum and UroLift are being compared as similar “minimally invasive” treatments. This MTG excludes consideration of	Thank you for your comment. The committee considered your comment carefully, and acknowledged that adverse

				important evidence distinguishing these therapies from each other: a) post-operative urinary retention, requirement for catheterisation, catheter-associated complications, UTI and urosepsis; and b) sexual dysfunction. • CATHETERISATION. Almost all patients who undergo treatment with Rezum are catheterised; reportedly from the studies for an average of 3-4 days; although the responses to the 30-NHS patient Rezum patient questionnaires in the MT413 Rezum Supporting documentation, suggests a much longer duration of catheterisation of 1-2 weeks. catheter-associated urinary tract infection (CAUTI) and bloodstream infection (CABSI) are leading causes of healthcare-associated infection in the NHS. According to NHS England, urinary tract infection (UTI) is the most common Health Care Associated Infection (HCAI), accounting for 17.2% of all HCAIs, with between 43% and 56% of UTIs associated with an indwelling urethral catheter. Patients with invasive devices such as urinary catheters are at a greater risk of developing an infection (NICE, 2012). In addition to increased costs, each one of these infections means additional use of NHS resources, greater patient discomfort and a decrease in patient safety [Source: https://www.england.nhs.uk/wp-content/uploads/2015/04/10-amr-lon-reducing-hcai.pdf]. A recent study to quantify the economic burden of CAUTIs found that each catheter is associated with an average 0.04 excess hospital-onset CAUTIs, 0.003 excess hospital-onset CABSIs, £30 in excess direct hospital costs, and a further 0.006 lost QALYs valued at £112 [Smith et al. J Hosp Infection 103 (2019) 44-54] • UTI and RETENTION: The AEs reported from real world experience with Rezum appear to have been discounted, despite a consistency with their findings. The high rate of AEs is consistent with that seen after TUNA and Microwave thermal ablation; both with very similar mechanisms of action to Rezum in terms of thermal ablation. Thermal ablation causes acute oedema leading to acute retention . It is disappointing that this MTG does	events were reported for each of the key studies during the assessment. Catheterisation: The committee was aware that that the need for and/or duration of catheterisation was defined as a patient outcome, but catheterisation is not described as an adverse event of Rezum. Section 4.5 describes the expert advice on adverse event after Rezum received by the committee. UTI and Retention: The committee noted the published evidence UTI rates which vary across the studies and the expert advice received based on their use of the technology in the NHS and decided not to change the guidance. Urosepsis: The committee noted that 1 case of urosepsis was reported in the Rezum II RCT crossover group. The clinical experts advised that side effects and complications after the Rezum procedure, some of which are similar to those after other treatments. The committee decided to make a minor change to section 4.5 to clarify this and to note the risk of urosepsis. (see section 4.5). Sexual function: The committee discussed the impact of Rezum on sexual function and decided to change the guidance. Please see the response to comment 34.

				not consider the results of prior thermal ablation technology – RF (TUNA) and microwave (TUMT) – neither adopted into the NHS in a meaningful way. The large retrospective observational study with Rezum (Mollengarden) showed a high rate of urinary tract infection and urethral stricture: Adverse events UTI: 17.1% Urinary retention: 14.0% Urethral stricture: 3.9% Postvoid dribbling: 3.9% Urinary incontinence: 3.9% Erectile dysfunction: 3.1% Retrograde ejaculation: 3.1% Additional BPH surgery: 2.3% Prostate tissue sloughing:1.6% Epididymo-orchitis: 1.6% Bladder stone: 0.8% Bladder neck contracture: 0.8% Similarly, data from 150 patients, presented at conference by the Mayo clinic [Yang DY et al. Abstract presented at AUA conference. 2018. MP33-21 Mayo Clinic pilot experience with Rezum prostate ablation] found 'higher than expected rates of UTIs' which influenced patient counselling and post procedure antibiotic regimen. The UTI rate was 14%, with 5.3% of patients requiring hospitalisation. • UROSEPSIS. Anecdotal reports of urosepsis are starting to emerge from NHS hospitals that are using Rezum. Rezum II reported one case of urosepsis, and a presentation on the real-world experience from one NHS hospital also reported on one patient who required HDU admission for a grade 4a UTI [Johnston M. Abstract MP01-03. Rezum water vapour ablation therapy for benign prostatic hyperplasia: Initial results from the UK. J Urol. 2019; 201 (4S)]. Duration of catheterisation for more than 3 days has been shown to be a significant risk factor for sepsis (p <0.0001) [Schneidewind et al. Cent European J Urol. 2017; 70: 112-117]	

				• SEXUAL FUNCTION. All thermal ablation procedures, including steam, have shown collateral damage of the prostate that leads to sporadic loss of ejaculatory function. MTG529 does not consider this important side effect and in fact assumes it to be the same as UroLift, which is the only treatment for BPH to never have a patient to have lost ejaculatory function in any report. The Rezum data is similar to the prior thermal ablation procedures because the mechanism of action is the same. Collateral damage to the bladder neck, ejaculatory ducts, and/or tissue surrounding the veru montanum are all potential causes of inconsistent results. The Rezum II study report avoids stating that Rezum preserves ejaculatory function because it does not reliably do so. While mean MSHQ-EjD scores were stable and even showed some improvement, 2.9% patients completely lost function (anejaculation) and 2.9% experienced “reduced ejaculatory volume”. This is similar to the 3.1% anejaculation reported by Mollengarden et al in the real world study of Rezum (Prostate Cancer Prostatic Dis. 2018 Sep;21(3):379-385). It is inappropriate to report adverse events simply as mean scores, since this hides low rates. If incontinence were treated this way, we would not acknowledge the possibility for incontinence after HoLEP or TURP, since mean scores stay largely level. This collateral damage associated with thermal ablation can be increased with more aggressive ablation, as seen in a report from the Mayo Clinic. Yang et a,l from the Mayo Clinic, reported 20% anejaculation after Rezum; this was presented at conference [Yang DY et al. Abstract presented at AUA conference. 2018. Poster UP3-33 Prevalence of Ejaculatory Dysfunction Following Rezum Prostate Ablation] and is described in a comparison of Rezum and UroLift [Kaplan SA. Demistifying less-invasive solutions for BPH. Urology Times. Sept 2019]. Ines et al conducted a more in-depth report of sexual dysfunction after Rezum, showing 17% anejaculation [Ines M et al. A retrospective review of the Rezum System: Treatment for benign prostatic hyperplasia in men with mild, moderate and severe lower urinary tract symptoms. NSAUA Sept 2019]. Many NHS patients elect to have UroLift treatment	

				instead of more invasive treatments in order to preserve sexual function. To not warn these men that Rezum does not offer the same certainty is a disservice to patients in whom these outcomes are important.	
74	5	Lay person	Evidence: Relevant evidence comes from 4 studies presented in 10 publications, including 1 randomised controlled trial	These studies do not appear to systematically examine adverse events to determine common causes. None of these studies, to my knowledge, addresses problems with overtreatment. More studies are needed as to the actual effect of the Rezum treatment on prostate tissue and nerves.	Thank you for your comment. The committee considered your comment carefully, and acknowledged that adverse events were reported. The committee was aware that none of studies reported any adverse events related to over using steam injections. The committee agreed to add a research consideration noting the potential value of evidence on the number of injections used in clinical practice and their associated side effects (see section 4.15).
75	5	Lay person	Committee discussion: Rezum is an effective minimally invasive procedure with clinical benefits	At this early stage of clinical use of Rezum the NHS should consider placing a limitation on the number of Rezum treatments that can be administered to an individual patient. Examination of the adverse events data on MAUDE suggests that there is a correlation between a high number of Rezum treatments and adverse events. An upper limit on the number of Rezum treatments would protect the public as additional clinical data is developed. There is a clear ability with the Rezum system to administer additional treatments at a future time if circumstances warrant. The Rezum instructions for use should be revised to reflect a precautionary bias.	Thank you for your comment. The committee considered your comment carefully, and acknowledged that the FDA MAUDE data is summarised in section 6 of the assessment report. The EAC advised that the FDA states that their medical device report data alone "cannot be used to establish rates of events, evaluate a change in event rates over time or compare event rates between devices. The number of reports cannot be interpreted or used in isolation to reach conclusions about the existence, severity, or frequency of problems associated with devices." The fact that there is no denominator figure of total procedures undertaken means these MAUDE reports cannot be set in context of all patients treated with Rezum in the USA. Please see the response to comment 25.
76	5	Lay person	Committee discussion: Rezum is unlikely to damage surrounding tissue and nerves,	To begin, I am a patient that reported an adverse event in 2019 to the FDA under the MAUDE system. Although I am not a citizen of the UK, I appreciate the opportunity to comment. Section 4.3 fails to grasp that the MORE treatments a patient receives with the Rezum device, the	Thank you for your comment and sharing your experience using Rezum with us. Please see the response to comment 25.

			and sexual function is not affected in the short term	MORE LIKELY it is that damage will be done to prostate tissue and nerves. This has been my experience. The manufacturer essentially ignores this simple truth in their advocacy for and evaluation of the Rezum system. The Rezum instructions for use do not require the practitioner to match the number of Rezum treatments to the size of the patient's prostate. This is a serious deficiency in the Rezum instructions for use.	
77	5	Lay person	Commission discussion: Rezum is unlikely to damage surrounding tissue and nerves, and sexual function is not affected in the short term	Section 4.3 states in part that the clinical experts "...explained that Rezum involves injecting steam into carefully directed and localized areas of the prostate from the inner, urethral surface of the prostate, and this may avoid nerve damage." The NICE reviews should note that this is essentially a naked claim without proof. The clinical trials do not cover this point at all, nor do the Rezum instructions for use.	Thank you for your comment. The committee considered your comment carefully, and acknowledged the statement is based on clinical experts' experience. The committee decided to make a minor change in section 4.3 to state possible damage to surrounding nerves.
78	7	NHS professional		UTI and sepsis rates are significantly higher for Rezum (one study published UTI rates up to 18%)	Thank you for your comment and sharing this information with us. Please see response to comment 73.
79	8	NHS professional		Having just stated that there was a case of Urosepsis after Rezum how did the experts come to this conclusion?	Thank you for your comment. Please see the response to comment 73 regarding urosepsis. The committee decided to make a minor change to section 4.5 to clarify this and to note the risk of urosepsis.
80	8	NHS professional		Mollengarden reported 4 cases of erectile dysfunction after Rezum treatment	Thank you for your comment. The committee agreed this is correct. Please see the response to comment 7.
81	8	NHS professional		In the Mollengarden paper UTI rate was 17%, not 5-7%. In addition most patients had an indwelling catheter for 4 days and the risk of catheter related UTIs is common after 3 days. I doubt that any modern microbiologist would advocate 5-7 days prophylactic antibiotics	Thank you for your comment. The committee considered your comment carefully. Please see response to comment 73. The committee decided to make amendments to section 4.5 of the guidance to clarify that the experts estimate of 5% to 7% risk refers to UTIs associated with a urinary catheter and to rephrase the reference to 5-7 days prophylactic antibiotics to a short course of prophylactic antibiotics.
82	4	NHS professional		I would estimate the risk of significant post-operative symptoms higher, at about 30%. The clinical improvement	Thank you for your comment and sharing your clinical experience. Clinical experts

				usually occurs after 3-4 months and I inform the patients appropriately.	confirmed that with Rezum the clinical improvement occurs sometime after the procedure. Further expert advice to the committee was that complications after the Rezum procedure are similar to those after other procedures for LUTs due to BPH. The committee decided to amend section 4.5 to clarify this.
83	9	NHS professional		- For prostate sees more than 80cc a HoLEP should be considered - Rezum at this stage should not be offered as a 1st line treatment for patient in urinary retention (poor evidence and retention patients were not included in the pivotal trial)	Thank you for your comment. Please see the responses to comments 2 and 18.
84	9	NHS professional		In our large cohort series - there was approximately a 10% incidence of retrograde ejaculation and a 1% incidence of erectile dysfunction. So patients should be warned about this and appropriately counselled that there a much smaller chance of sexual dysfunction (not zero % as the recommendation text implies)	Thank you for your comment and sharing your clinical experience with us. Please see the response to comment 7.
Others (n=12)					
85	1		Consultation question	*Are there any equality issues that need special consideration and are not covered in the medical technology consultation document?* Uncertain	Thank you for your comment.
86	2		Consultation question	*Are there any equality issues that need special consideration and are not covered in the medical technology consultation document?* None	Thank you for your comment.
87	4		Consultation question	*Are there any equality issues that need special consideration and are not covered in the medical technology consultation document?* Not to my knowledge	Thank you for your comment.
88	8		Consultation question	*Are there any equality issues that need special consideration and are not covered in the medical technology consultation document?* None	Thank you for your comment.
89	9		Consultation question	*Are there any equality issues that need special consideration and are not covered in the medical technology consultation document?* No	Thank you for your comment.

90	10		Consultation question	*Are there any equality issues that need special consideration and are not covered in the medical technology consultation document?* None that we are aware of	Thank you for your comment.
91	3	Manufacturer	General	We welcome the committees positive guidance decision for Rezum.	Thank you for your comment.
92	7	NHS professional		As a urologist with an active interest in BPH treatments, and who provides HoLEP, Urolift and Rezum and has been involved in trials of novel BPH therapies, I feel well placed to respond to some of the aspects of this consultation.	Thank you for your comment
93	8	NHS professional		Popular demand driven by the Daily Mail rather than by the World literature	Thank you for your comment.
94	8	NHS professional		There are multiple examples in the document that quote 'expert opinion' which is not evidenced in the Medical technologies guidance - Collated expert questionnaires from the 8 experts. From whom and where did these references come?	Thank you for your comment. The committee considered your comment carefully. The process guide for NICE medical technology guidance describes the role of expert advisers in guidance development and how they are recruited. Alongside the expert questionnaires the experts provide advice to the EAC, the lead team and the committee. .
95	8	NHS professional	Expert opinion indicated that recruiting participants to clinical trials that directly compare different minimally invasive and invasive treatments is challenging because people often express a preference to avoid more invasive treatment.	Where did this expert opinion come from? Certainly recruitment to any RCT comparing different surgical treatments is not easy but there is a need for this certainty of evidence before treatments come into widespread practice. This NICE document could result in greater than 10,000 patients receiving this treatment within 12 months on the basis of poor evidence and weak conclusions.	Thank you for your comment. Please see the response to comment 94.
96	5	Lay person	The Rezum procedure is easy to learn	The Rezum manufacturer, through the assistance of a contractor, has developed a training device for the Rezum device which may also include training videos and other instructions. These materials are not available to the	Thank you for your comment and sharing your experience with us. The committee considered your comment about training and the dangers of

				public. It is completely unknown whether the training matches the Rezum instructions for use. Of particular concern should be issues of proportionality in treatment, estimation of the appropriate number of Rezum treatments in various circumstances and the potential for overtreatment. At one point in the recent past, the Rezum manufacturer changed the instructions for use to add a caution regarding overtreatment. The reasons for this change should be investigated by the NICE evaluators. The Rezum manufacturer has refused to provide me, as a patient, information on overtreatment.	overtreatment. It was aware of the lack of evidence on the association between the number of injections and side effects, and agreed to add a consideration noting the value of this research work (see section 4.15).
Research (n=2)					
97	8	NHS professional	Further research	should be compulsory and essential	Thank you for your comment.
98	9	NHS professional		Also further research is needed to evaluate the role of Rezum in managing patients with urinary retention.	Thank you for your comment. Please see the responses to comments 2 and 18.

Appendix 1: EAC additional review and analysis

Additional studies quoted in the consultation comments

There are additional studies cited in the consultation comments (comment 19, 20, 23, 24), many of which report data for one of Rezum's comparator (UroLift), in challenging the accuracy of various statements made in the Rezum draft guidance. The EAC has reviewed these studies and provides a summary of individual studies in the comments in Table 1. These studies should be considered with caution, as most were not identified in the systematic literature search undertaken by the EAC during the assessment because they reported data on comparators only, or because they were abstracts and thus not fully appraisable. Rather, they have been identified by consultees using a non-systematic approach and may therefore be subject to bias.

An important study that warrants further discussion is the MedLift study by Rukstalis et al. (2018) [1]. This study had not been previously identified by the EAC because it only concerns the comparator, UroLift. The MedLift was a prospective single-armed study conducted using the FDA Investigational Device Exemption (IDE) scheme. Patients were enrolled according to the same inclusion and exclusion criteria as the LIFT study [2], with the exception that all the patients had obstructive middle lobes, with the aim of the study being to investigate the efficacy and safety of the device in these patients. Forty five patients were enrolled with a follow up of 12 months. The study reported that patients experienced a mean improvement in their international prostate symptom score (IPSS) of 13.5 compared with baseline ($p < 0.0001$). There were also significant improvements in quality of life, BPH Impact Index (BPHII) and peak flow rate (Qmax), whilst erectile and ejaculatory function were preserved. Results were at least as good as historical data in patients with lateral lobe enlargement from the LIFT study. Of note, regarding the economic case, the treatment of the obstructive middle lobe with UroLift was associated with an increased number of implants per subject from a mean of 5.1 (± 2.2 SD) in the active arm of the LIFT study (lateral lobe only) to 6.3 (± 1.6 SD) in MedLift ($p = 0.0005$).

This study demonstrates that UroLift may be used in patients with median lobe enlargement as well as patients with lateral lobe enlargement. This is reflected in the company's Instructions For Use (IFU) which now includes this indication. Thus, the EAC's statement in the Assessment Report (Section 8.1, page 52) that "the Rezum procedure allows for treatment of patients with median lobe or elevated central zone hyperplasia, who are currently contraindicated to treatment with UroLift" should be disregarded.

Rezum indication: people with urinary retention

During the consultation, the consultees (comment 2 and 9) suggested that Rezum may not suitable for people with urinary retention. The EAC has reviewed the included studies to check if people in urinary retention were included in the study populations.

The inclusion or exclusion of urinary retention was not reported in the Rezum II trial [3]. The protocol for the trial (NCT01912339) lists the following exclusion criteria:

- Post-void residual (PVR) > 250 ml.
- Subjects who have had an incidence of spontaneous urinary retention either treated with indwelling transurethral catheter or suprapubic catheter six months prior to baseline. A provoked episode now resolved is still admissible."

Therefore patients with urinary retention were excluded, although post-procedural *de novo* retention was reported. The retrospective study by Mollengarden [4] had the same exclusion criteria as the Rezum II study. No information was reported on urinary retention status in the study by Dixon et al. [5]. The retrospective study by Darson et al. (2017) stated urologist included patients for treatment with Rezum at their discretion, with 3/131 (2.3%) being described as being in retention [6]

The EAC also checked the Instructions for Use (IFU), and urinary retention is not listed as a contra-indication in the IFU. The EAC noted that patients with BPH exhibiting urinary retention was not a subgroup identified in the scope of the assessment.

Study population of the Rezum II study

The consultees (comment 33 and 36) noted that only about 51% of people initially investigated (i.e. screened for eligibility) were included in the Rezum II trial and questioned the generalisability of study population.

The EAC has checked the inclusion and exclusion criteria for the Rezum II trial and indicated that randomised controlled trials do tend to have strict inclusion criteria so that many people are found to be ineligible following screening. The reasons for exclusion of the 187/384 (49%) in Rezum II were not reported, but given there were 35 exclusion criteria detailed in the protocol (NCT01912339), it is perhaps not surprising that around half of screened patients did not meet the eligibility criteria. For comparison, in the LIFT trial [7], which had nearly identical methodology and reporting standards, 206/430 were included following screening (i.e. 53% excluded). In contrast, the exclusion criteria for this study's protocol were vague "Size, volume, length of prostate" (NCT1294150).

Retreatment rate using Rezum

The consultees (comment 25 and 32) considered that the retreatment rate of Rezum was underestimated while UroLift rate was overestimated. The EAC has checked the retreatment rate of Rezum and Urolift noted in the included studies and new real world data on UroLift, cited in the consultation comments [8].

The EAC considered that the most reliable data and certainly the most comparable were from the Rezum II and LIFT studies. Whilst the EAC noted the attrition rate in the Rezum trial over 4 years was high (34%) [9], it was comparable to that of the LIFT study (38% over 5 years) [2]. The EAC did not observe any evidence that the rate was underestimated for Rezum and/or overestimated for UroLift. Furthermore, the clinical experts were unanimous that the differing mechanisms of action provided a plausible reason for Rezum's superiority in this regard.

A large retrospective observational study has been published on UroLift (n = 1413) [8]. Despite being reported as a 2 year study, the mean follow up was only 273 days. The study reported that 72 patients had retreatment. However, as neither the denominator nor survival analysis (Kaplan Meier) were reported, it is not possible to calculate a retreatment rate from these data. Additionally, the EAC has not identified an equivalent real-world study in Rezum. Therefore it is the opinion of the EAC that data from Rezum II and LIFT trials, used in the indirect comparison submitted by the company, are the most robust for use in the economic model, despite their limitations.

The number of injections used in Rezum

The consultees (comment 18, 54 and 55) indicated that a high number of steam injections is associated with adverse events. The EAC has reviewed included studies to examine if adverse events may be associated with the number steam injections used in the Rezum procedure.

The EAC did not identify any study that investigated the association between the number of steam applications and adverse effects. The number of steam applications was reported in all the included studies as follows:

- Rezum II trial [3]: 4.5 (±1.8 SD)
- Dixon et al. (2015) [5]: 4.6 (range 2 to 9)
- Mollengarden et al. (2018) [4]: 5.5 (± 2.1 SD)
- Darson et al. (2017) [6]: 4.4 (range 2 to 12).

Most patients receive between 4 and 5 injections, and the most used in the studies was 12. The clinical experts suggested that if a particularly large number of injections

were required (for a very large prostate), a different procedure should be used (typically TURP or HoLEP).

Additional cost modelling (using updated clinical parameters)

The consultees noted that the clinical parameters used in the cost modelling for one of Rezum's comparators (UroLift) were based on the published guidance (comment 40, 42,47 and 51), and these may not reflect current clinical practice. The EAC has explored the changes of clinical parameters (quoted in the consultation comments) and examined the potential impact on the cost saving (using the most up to date clinical parameters when necessary in the cost modelling). The following clinical parameters include:

- The cost of technology (in terms of UroLift:, the cost increase based on consumer price inflation and a nominal range of percentage increase in the cost of UroLift based on the MTG26, i.e. 10%, 20% and 30% increase).
- Number of UroLift implants
- The length of hospital stay
- Duration of the procedure.
- To include the cost of an appointment for catheter removal.
- Retreatment rate

The EAC has reported additional analyses to reflect these scenarios in Table 2. The scenario analysis shows that, when done individually, changing each parameter to the suggested alternative parameter did not change the direction of results using deterministic analysis. Additionally, PSA indicated that it was highly probable Rezum remained cost saving compared with UroLift for each individual change. The EAC could not apply PSA to the cost of catheter removal and did not change the retreatment rates as there were no plausible estimates identified to replace the existing values.

However, when all the changes were combined (i.e. the best possible scenario in favour of UroLift) in Table 3, deterministic analysis showed UroLift was cost-saving in the base case, and very slightly cost-saving when the cost of a UroLift implant was increased by 10% of the UroLift price in the Urolift guidance (£330 excluding VAT). Rezum remained cost saving when the cost of UroLift was increased by 20% or 30% of the published UroLift cost. In each case, PSA demonstrated the 95% credibility intervals crossed zero (cost neutrality), indicating there was residual uncertainty over the true direction of cost savings of the technologies.

Table 1: Brief description of studies noted by commentators.

Comment number	Study ID (from commentator)	Retrieved?	Study description	EAC Comment
19	1) AUA conference. 2018. Poster UP3-33 Prevalence of Ejaculatory Dysfunction Following Rezum Prostate Ablation] 2) Kaplan SA Demistifying less-invasive solutions for BPH. Urology Times. Sept 2019 3) Ines M et al. A retrospective review of the Rezum System: Treatment for benign prostatic hyperplasia in men with mild, moderate and severe lower urinary tract symptoms. NSAUA Sept 2019	1) Yes, this study is Yang et al. (2019) 2) Yes, News article, review 3) Yes, Poster abstract.	1) **Abstract** Retrospective chart review (n=81) with telephone survey (43 patients responded). 11 patients (described as 20%) reported retrograde ejaculation or anejaculation. The authors concluded potential Rezum patients should be counselled about these risks. 2) N/A 3) **Abstract** Retrospective observational study Single-armed retrospective observational study of men (n=152. receiving Rezum, 12 months follow up. The abstract is positive about the benefits of Rezum. The pertinent point made by the commentator is it is reported that 19/110 men (17.3%) experienced "complete loss of ejaculatory fluid" in Table 2.	Two of these studies report the rate the rate of ejaculatory complications is higher than was reported in the Rezum II trial or the included fully published observational studies. However, these studies should be treated with caution as they were published in abstract form only and were not subject to peer-review. Without having access to the full study information, it is difficult to contextualise these results, for instance understanding the severity of the adverse events.
20	MedLift study, Rukstalis et al. (2019)	Yes, here.	**Full study** FDA investigational device exemption (IDE) extension of the LIFT study (single armed, n = 45). The study appears to show that UroLift can be used to treat the middle lobe of the prostate as effectively as it treats lateral lobes.	This is a study published after the publication of UroLift guidance of UroLift. The study is on the comparator of Rezum and is out of the scope for Rezum guidance. The study provides evidence that UroLift (Rezum

Comment number	Study ID (from commentator)	Retrieved?	Study description	EAC Comment
				comparator) can be used in patients with obstructive median lobes. Data on the number of implants in these subjects may further inform the discussion on UroLift device costs for economic modelling.
24 and 26	Guo DP et al. Int J Urol 2017;24:703-707	Yes, here	**Full study** Retrospective observational study reporting the natural history of men with with urinary retention (n=67, 3 year follow up).	This study provides background information on urinary retention only no intervention or comparator. It is out of the scope of Rezum.
32	• "If compared to a larger series of Urolift patients (real world data study published Sep 2019)" [The EAC assume this refers to the study by assume this means Eure study (2019) [reference 8]. The EAC has discussed the context of this study in 4.	Yes, here	**Full study** Retrospective chart review (n=1413) of patients receiving UroLift.	In the opinion of the EAC, this study did not provide useful comparative data or data informative to the economic model, and it is out of scope.
42	• [REGARDING THEATRE TIME] • • 1) 10 mins reported by Leeds NHS Trust [Poster presented at WCE 2018. Young M. Transforming BPH surgical care to an ambulatory setting - what are the gains and losses?], • • 2) 25 mins reported by Norfolk and Norwich University Hospital, based experience with 250	1) Yes, here 2) Yes 3) Yes 4) Yes.	1) **Abstract** Economic model comparing UroLift with Bi-TURP 2) **Webpage** NICE shared learning database 3) **Abstract** Poster. Retrospective observational costing study (n=20) comparing UroLift with TURP (n=20).	1) This study reports a procedural time of 9 minutes for UroLift. However, it is not known how this value was derived. 2) This shared learning example does specify a theatre time of 25 minutes for UroLift. 3) No information on procedural duration is presented in this abstract.

Comment number	Study ID (from commentator)	Retrieved?	Study description	EAC Comment
	patients [https://www.nice.org.uk/sharedlearning/adoption-of-urolift-procedure-an-ambulatory-pathway-for-patients-suffering-from-lower-urinary-tract-symptoms-of-benign-prostatic-hyperplasia], • • 3) 20 mins reported by Northampton General Hospital [poster presented at BAUS 2019. Carrie A and Nemade H. Comparative cost effectiveness of Urolift procedure vs TURP.] • • 4) 20-30 mins reported by Royal Devon & Exeter [https://www.nice.org.uk/sharedlearning/urolift-a-community-based-alternative-treatment-for-benign-prostatic-obstruction-bpo].		4) **Webpage** NICE shared learning database	4) This shared learning example does specify a theatre time of 20-30 minutes for UroLift. All these studies are out of scope.
52	• [REGARDING CATHETERISATION] • • 1) A recent study to quantify the economic burden of CAUTIs found that each catheter is associated with an average 0.04 excess hospital-onset CAUTIs, 0.003 excess hospital-onset CABSIs, £30 in excess direct hospital costs, and a further 0.006 lost QALYs	1) Yes 2) Yes.	1) **Full paper** Economic study concerning the burden of catheterisation. 2) **Abstract** Retrospective chart review (n=81) with telephone survey (43 patients responded).	1) The study is of limited applicability to the decision problem, and is out of scope. 2) The EAC did not identify data from this abstract on UTI rates.

Comment number	Study ID (from commentator)	Retrieved?	Study description	EAC Comment
	valued at £112 [Smith et al. J Hosp Infection 103 (2019) 44-54] • • [REGARDING UTI AND RETENTION] • • 2) Similarly, data from 150 patients, presented at conference by the Mayo clinic [Yang DY et al. Abstract presented at AUA conference. 2018. MP33-21 Mayo Clinic pilot experience with Rezum prostate ablation] found 'higher than expected rates of UTIs' which influenced patient counselling and post procedure antibiotic regimen. The UTI rate was 14%, with 5.3% of patients requiring hospitalisation.			
52	[REGARDING UROSEPSIS] 1) Johnston M. Abstract MP01-03. Rezum water vapour ablation therapy for benign prostatic hyperplasia: Initial results from the UK. J Urol. 2019; 201 (4S) 2) Duration of catheterisation for more than 3 days has been shown to be a significant risk factor for sepsis (p <0.0001) [Schneidewind et al. Cent European J Urol. 2017; 70: 112-117] [REGARDING SEXUAL FUNCTION]	1) Yes here (MP01-03) *. 2) Yes, here 3) Yes. News article, discussed in comment 19.	1) **Abstract** Prospective observational study (n=181). "Results of this UK experience with the Rezum minimally invasive procedure confirms an early response to treatment with significant relief of LUTS and low morbidity". One patient had a grade 4a UTI requiring admission, as highlighted by the commentator. 2) **Full paper** Retrospective observational study on UTI following TURP.	1) This study was identified and included in the Assessment Report. It requires caution as is reported in abstract form only. 2) The study is of limited applicability to the decision problem.. 3) See comment 19.

Comment number	Study ID (from commentator)	Retrieved?	Study description	EAC Comment
	3) "This collateral damage associated with thermal ablation can be increased with more aggressive ablation, as seen in a report from the Mayo Clinic….. and is described in a comparison of Rezum and UroLift [Kaplan SA. Demistifying less-invasive solutions for BPH. Urology Times. Sept 2019].		3) See comment 19.	

Table 2: The cost difference per treatment between Rezum and UroLift by individual clinical parameters

Scenario	#	Change	Cost difference per patient (Rezum – UroLift) at 4 years		Comment
			Deterministic £	Probabilistic, Mean £ [95% CI] from 1000 simulations	
EAC Base-case	-	-	**-£497**	**-£511 [-£1022, -£1]**	Cost saving of Rezum (vs UroLift) is small when compared to the large uncertainty in model (Table 9.9 EAC Report).
EAC Base-case	-	UroLift bundled cost not varied (i.e. fixed) in PSA	**-£497**	**-£513 [-£906, -£191]**	By fixing UroLift costs, the uncertainty reduces slightly.
Cost of UroLift implants	**1a**	£349.47 (£330+CPI inflation) in EAC Base-case, **increased by 10%** per implant*	-£614	-£622 [-£1020, -£295]	Total device costs for UroLift were the subject of threshold analysis in the EAC assessment report (Figure 9.7).
	1b	£349.47 (£330+CPI inflation) in EAC Base-case, **increased by 20%** per implant*	-£728	-£739 [-£1134, -£401]	

	1c	£349.47 (£330+CPI inflation) in EAC Base-case, **increased by 30%** per implant*	-£842	-£843 [-£1269, -£482]	
Number of UroLift implants	**2**	4.4 UroLift implants applied in EAC Base-case, **reduced to 4.0** implants used per patient*	-£353	-£347 [-£734, -£9]	Total device costs for UroLift were the subject of threshold analysis in the EAC assessment report (Figure 9.7).
Hospital length of stay	**3**	0.5 days for UroLift and Rezum in EAC Base-case, **reduced to 0.125 days for UroLift only***	-£356	-£353 [-£725, -£18]	Hospital length of stay was the subject of threshold analysis in the EAC assessment report (Figure 9.9).
Theatre time	**4**	Rezum 17.5 minutes, UroLift 30 minutes in EAC Base-case, **both changed to 20 minutes***	-£325	-£326 [-£647, -£6]	Procedural duration was the subject of sensitivity analysis in the EAC assessment report (Figure 9.8, Tables 9.10, 9.11).
Catheter removal	**5**	The cost of catheter removal was not included in original model, add £144 [HRG LB15E OPROC] to total bundled Rezum device costs*. Note Rezum bundled cost not varied (i.e. fixed) in PSA	-£351	-£358 [-£719, -£11]	HRG code* LB15E is an average bundled cost reflecting a varied case mix of procedures, some of which are likely to be more complex than a standard TWOC. Large uncertainty in cost and proportion of patients it applies to in each arm. * Note: an HRG code is a method of paying a tariff fee to a provider (such as a hospital trust) for a service performed, as part of payment by results (PbR). This may not represent the true cost of the procedure to the NHS.

Retreatment rates	**6**	Rates taken from the best comparable evidence. Unchanged	EAC Base-case unchanged	EAC Base-case unchanged	
Key: green=Rezum cost saving, red=Rezum cost expending, *UroLift bundled cost not varied (i.e. fixed) in PSA					

Table 3: The cost difference per treatment between Rezum and UroLift when all clinical parameters are combined in best possible scenario to favour UroLift

Scenario	#	Change	Cost difference per patient (Rezum – UroLift) at 4 years		Comment
			Deterministic £	Probabilistic, Mean £ [95% CI] from 1000 simulations	
EAC Base-case	-	-	**-£497**	**-£511 [-£1022, -£1]**	Cost saving of Rezum (vs UroLift) is small when compared to the large uncertainty in model (Table 9.9 EAC Report).
EAC Base-case	-	UroLift bundled cost not varied (i.e. fixed) in PSA	**-£497**	**-£513 [-£906, -£191]**	By fixing UroLift costs, the uncertainty reduces slightly.
Combined scenarios from Table 2	**2,3,4,5**	Number of implants, hospital length of stay, theatre time, catheter removal altered (UroLift device costs unchanged)*	+£107	+ £122 [-£182, +£421]	Interval crosses 0.
	1a,2,3,4,5	UroLift implant cost increases by 10%, number of implants, hospital length of stay, theatre time, catheter removal altered*	+£2	+£8 [-£279, +£313]	Interval crosses 0.
	1b,2,3,4,5	UroLift implant cost increases by 20%, number of implants, hospital length of stay, theatre time, catheter removal altered*	-£102	-£89 [-£384, +£209]	Interval crosses 0.
	1c,2,3,4,5	UroLift implant cost increases by 30%, number of implants, hospital length	-£205	-£199 [-£504, +£101.81]	Interval crosses 0.

		of stay, theatre time, catheter removal altered*			
Key: green=Rezum cost saving, red=Rezum cost expending, *UroLift bundled cost not varied (i.e. fixed) in PSA					

References

1. Rukstalis D, Grier D, Stroup SP, Tutrone R, deSouza E, Freedman S, et al. Prostatic Urethral Lift (PUL) for obstructive median lobes: 12 month results of the MedLift Study. Prostate Cancer Prostatic Dis. 2019 Sep;22(3):411-9.
2. Roehrborn CG, Barkin J, Gange SN, Shore ND, Giddens JL, Bolton DM, et al. Five year results of the prospective randomized controlled prostatic urethral L.I.F.T. study. The Canadian journal of urology. 2017 Jun;24(3):8802-13.
3. McVary KT, Gange SN, Gittelman MC, Goldberg KA, Patel K, Shore ND, et al. Minimally Invasive Prostate Convective Water Vapor Energy Ablation: a Multicenter, Randomized, Controlled Study for the Treatment of Lower Urinary Tract Symptoms Secondary to Benign Prostatic Hyperplasia. J Urol. 2016;195(5):1529-38.
4. Mollengarden D, Goldberg K, Wong D, Roehrborn C. Convective radiofrequency water vapor thermal therapy for benign prostatic hyperplasia: a single office experience. Prostate Cancer and Prostatic Diseases. 2018;21(3):379-85.
5. Dixon C, Cedano ER, Pacik D, Vit V, Varga G, Wagrell L, et al. Efficacy and Safety of Rezum System Water Vapor Treatment for Lower Urinary Tract Symptoms Secondary to Benign Prostatic Hyperplasia. Urology. 2015;86(5):1042-7.
6. Darson MF, Alexander EE, Schiffman ZJ, Lewitton M, Light RA, Sutton MA, et al. Procedural techniques and multicenter postmarket experience using minimally invasive convective radiofrequency thermal therapy with Rezūm system for treatment of lower urinary tract symptoms due to benign prostatic hyperplasia. Research and reports in urology. 2017;9:159-68.
7. Roehrborn CG, Gange SN, Shore ND, Giddens JL, Bolton DM, Cowan BE, et al. The prostatic urethral lift for the treatment of lower urinary tract symptoms associated with prostate enlargement due to benign prostatic hyperplasia: the L.I.F.T. Study. J Urol. 2013 Dec;190(6):2161-7.
8. Eure G, Gange S, Walter P, Khan A, Chabert C, Mueller T, et al. Real-World Evidence of Prostatic Urethral Lift Confirms Pivotal Clinical Study Results: 2-Year Outcomes of a Retrospective Multicenter Study. J Endourol. 2019 Jul;33(7):576-84.
9. McVary KT, Rogers T, Roehrborn CG. Rezum Water Vapor Thermal Therapy for Lower Urinary Tract Symptoms Associated With Benign Prostatic Hyperplasia: 4-Year Results From Randomized Controlled Study. Urology. 2019;126:171-9.