EUnetHTA Joint Action 3 2016-2020

Comparative effectiveness of surgical techniques and devices for the treatment of benign prostatic hyperplasia (BPH)

Project ID: ***OTCA27***

Project description and planning

Regione Emilia-Romagna (RER), Italy

Austrian Institute for Health Technology Assessment (AIHTA)

Version log

Version number	Date	Modification	Reason for the modification
V1	**07/05/2020**	First draft sent to co-authors	
V2	**02/06/2020**	Integration of comments and suggestions from co-authors	Review by co-authors
V3	**03/07/2020**	Integration of comments from scoping e-meeting and of grading of outcomes from GRADEpro survey	Scoping e-meeting and GRADEpro survey
V3	**06/07/2020**	Draft sent to dedicated reviewers	
V4	**13/07/2020**	Integration of comments and suggestions from dedicated reviewers	Review by dedicated reviewers
V4	**14/07/2020**	Draft sent to external experts	
V5	**30/07/2020**	Final version	Review by external experts

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1. Project organization

1.1 Participants

Table 1.1 Project participants

	Agency	Role in the project	Country	Distribution of work
Assessment team				
1	Regione Emilia-Romagna – RER	Author	Italy	• Develop the drafts and final version of EUnetHTA project plan • Set up the process for rating the relevance of outcomes and participate to the survey (GRADE method) • Perform the literature search & study selection • Carry out the assessment (extraction, quantitative and qualitative analyses, perform the network meta-analysis, synthesis and interpretation of findings) • Process all reviewers' comments and provide answers to the comments • Prepare final assessment and write a final summary of the assessment
2	Austrian Institute for Health Technology Assessment - AIHTA	Co-Author	Austria	• Collaboration in the development of the EUnetHTA project plan • Check, provide input and approve all steps • Participate in the rating of the relevance of outcomes (GRADE method) • Contribute to studies' data extraction and assessment of risk of bias • Development of the "Features of the intervention" (Core Model domain: "Description and technical characteristics of the technology") • Check, provide input and approve content of all domains, Discussion and Conclusions, which will be agreed upon • Review draft assessment, propose amendments where necessary and provide written feedback • Check and approve answers to the reviewers' comments prepared by the author
3	State Health Care Accreditation Agency under the Ministry of Heatlh of the Republic of Lithuania - VASPVT	Dedicated reviewer	Lithuania	• Review draft project plan, propose amendments where necessary and provide written feedback • Participate in the rating of the relevance of outcomes (GRADE method) • Review 1st draft assessment, propose amendments where necessary and provide written feedback
4	Swiss Network for Health Technology Assessment - SNHTA	Dedicated reviewer	Switzerland	• Review draft project plan, propose amendments where necessary and provide written feedback • Participate in the rating of the relevance of outcomes (GRADE method) • Review 1st draft assessment, propose amendments where necessary and provide written feedback

5	Azienda Zero Region Veneto	Dedicated reviewer	Italy	• Review draft project plan, propose amendments where necessary and provide written feedback • Participate in the rating of the relevance of outcomes (GRADE method) • Review 1st draft assessment, propose amendments where necessary and provide written feedback
Contributors				
6	Dr Franco Bergamaschi	External expert	Italy	• Provide input and review the project plan and the assessment drafts • Review methods, results, and conclusions based on the original studies included. Provide constructive comments in all project phases.
7	Dr Alfio Capizzi	External expert	Italy	• Provide input and review the project plan and the assessment drafts • Review methods, results, and conclusions based on the original studies included. Provide constructive comments in all project phases.
8	Dr Iain Robertson	External expert	Scotland	• Provide input and review the project plan and the assessment drafts • Review methods, results, and conclusions based on the original studies included. Provide constructive comments in all project phases.
9	Austrian Institute for Health Technology Assessment - AIHTA	Project manager	Austria	• Project management

1.2 Project stakeholders

Manufacturers of selected technologies will be involved only via a question-answer approach, should the publicly available information on their websites be insufficient for a detailed description of technology in sufficient detail. Patients and/or patient organisations involvement will be attempted using the Open call for patient input issued on the EUnetHTA website. Patient organisations will be actively contacted to provide input about the disease, living with the disease and personal experience with the technologies.

1.3 Milestones and deliverables

Table 1.3 Milestones and Deliverables

Milestones/Deliverables	Start date	End date
Project duration	**04.05.2020**	
Scoping phase	04.05.2020	31.07.2020
Identification of external experts; identification of patient organisations	04.05.2020	30.05.2020
Scoping and development of draft Project Plan incl. preliminary PICO	04.05.2020	30.05.2020
Internal Scoping e-meeting with the assessment team	17.06.2020	17.06.2020
Confirmation of list of outcomes and ratings of importance of outcomes (via GRADEpro)	22.06.2020	29.06.2020
Consultation of draft Project Plan with dedicated reviewers	06.07.2020	10.07.2020
Consultation of draft Project Plan with external experts	14.07.2020	21.07.2020
Amendment of draft Project Plan & final Project Plan available	30.07.2020	
Assessment phase	**31.07.2020**	**31.03.2021**
Writing first draft rapid assessment	23.07.2020	31.12.2020
Review by dedicated reviewer(s)	04.01.2021	22.01.2021
Writing second draft rapid assessment	25.01.2021	19.02.2021
Review by ≥ 2 external experts and fact check by manufacturers	19.02.2021	05.03.2021
Relaunch of literature search and updating	04.01.2021	05.03.2020
Writing third draft rapid assessment	08.03.2021	12.03.2021
Medical editing	15.03.2021	19.03.2021
Writing of fourth version of rapid assessment	22.03.2021	24.03.2021
Formatting	25.03.2021	30.03.2021
Final version of rapid assessment		**31.03.2021**

2. Project outline

2.1 Project objectives

The rationale of this multi-technology assessment is to collaboratively produce structured (rapid) core HTA information on minimally invasive surgical treatments for Benign Prostatic Hyperplasia (BPH). In addition, the aim is to apply this collaboratively produced assessment in the national and/or regional context.

Table 2.1 Project objectives

	List of project objectives	**Indicator (and target)**
1	To jointly produce health technology assessments that are fit for purpose, of high quality, of timely availability, and cover the whole range of health technologies.	Production of a (rapid) relative effectiveness assessment comparing different minimally invasive surgical treatments for BPH
2	To apply this collaboratively produced assessment into local (e.g. regional or national) context	Production of $\geq$ 2 local (e.g. national or regional) reports based on the collaboratively produced assessment

This rapid assessment will provide comparisons among different minimally invasive surgical treatments for BPH, in order to assess their relative effectiveness and safety in patients with indication for surgical treatment and different subpopulations, according to prostate size.

This topic was chosen based on a request from local decision makers who commissioned the authors' agency to carry out an HTA to assess the relative effectiveness and safety of minimally invasive surgical treatments compared to available alternatives. A specific interest was expressed for technologies included/recommended in guidelines from the European Association of Urology [1] and from the American Urological Association [2]. Additionally, the EUnetHTA Prioritization List for Other Technologies contains other innovative interventions, such as water vaporization and prostatic artery embolization (PAE), which are also proposed for the treatment of BPH. The topic resulted relevant to other partnering agencies that joined in a collaborative assessment team and decided to extend the scope for multiple technologies intended to treat BPH.

The relevance of the topic lies in the fact that new technologies are intensely marketed in both public and private institutions, but not yet widely introduced in the public sector and could have relevant organisational and economic impact on services for patients needing surgery for benign prostatic hyperplasia:

2.2 Project Method and Scope

2.2.1. Approach and Method

Table 2.2.1 Project approach and method

Project approach and method
A search for International guidelines, systematic and narrative reviews, UpToDate (https://www.uptodate.com) will be performed in order to fulfil information requested by "Health problem and current use" (CUR) domain [3]. The selection of assessment elements will be based on The HTA Core Model® for Rapid Relative Effectiveness Assessment Version 4.2 [3]. One high quality systematic review with network meta-analysis published in November 2019, including Randomized Controlled Trials (RCTs) comparing different treatments addressed in this report [4] was found and will constitute the starting point for this assessment and the basis for setting and updating the search for RCTs to answer questions on effectiveness and safety (EFF and SAF). RCTs comparing each of the technologies of interest vs sham procedures will be considered only if head to head comparative RCTs will not be found for those technologies. Systematic reviews will be also searched in order to double check for relevant RCTs. Treatments or technologies not addressed by the aforementioned systematic review will be searched using the same search strategy Publicly available information about the technologies identified to be relevant in the assessment will be used in the "Description and technical characteristics" of technologies under assessment (TEC) domain [3]. Should the information prove insufficient, the manufacturers of the respective technologies will be asked to provide additional information and non-confidential data. The database specific search strategies will be used to identify RCTs for "Clinical Effectiveness" (EFF) and "Safety" (SAF) domains [3]. References of systematic and non-systematic reviews will also be checked to identify additional RCTs that could be included. Four reviewers will carry out the study selection process, independently, in accordance with previously defined PICO question. Disagreement will be discussed and resolved between reviewers. A PRISMA flow chart reporting the studies selection process will be created. The data extraction process will be performed by five reviewers. Data collection form including information listed in the Preliminary evidence table (Table 2-4) will be used. Disagreement or consensus between reviewers on the eligibility of each study will be tracked in the data collection form. Quality assessment tools: quality of included studies will be assessed focusing mainly on "risk of bias" using the Cochrane risk of bias tool (RoB 2.0 tool) [5] as recommended by the EUnetHTA guideline "Internal validity of RCTs" [6]. The level of confidence/certainty in the body of evidence will be assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system [7].

During the Scoping phase external experts as well as authors and dedicated reviewers have been involved in selecting outcomes of interest and in grading the importance of each identified outcome. Relevant subgroup analyses will be performed for the critical outcomes.

A “Summary of findings” table will be created using GRADE Pro tool [8]. Quantitative analysis methods with meta-analysis and network meta-analysis where possible will be used for SAF and EFF domains. [9] Descriptive analysis of information will be performed for other domains.

Table 2-3: Planned literature search strategy

Literature search strategy
A systematic review of the scientific literature will be performed according to the Cochrane Handbook methodology - Version 2019 [9]. The Systematic Review production tool (RevMan 5) will be also used [10] for data extraction, risk of bias representation and SoF tables. As one high quality systematic review have been published in November 2019 [4] the systematic search will be performed in the following databases having January 2019 as a starting date: • Medline • Embase • Cochrane Library The search strategy developed for all the three databases will be the following: ("Prostatic Hyperplasia"[Mesh] OR "Lower Urinary Tract Symptoms"[Mesh]) OR "Prostatism"[Mesh] OR benign prostatic hyperplasia OR BPH OR lower urinary tract symptom* OR luts OR prostatism) AND (((thulium OR holmium OR diode OR eraser OR ktp OR greenlight) AND laser) OR KTP LVP OR Bipolar EP OR Bipolar VP OR bipolar transurethral resection OR Bipolar TURP OR plasmakinetic OR water vapour OR steam OR water vaporization OR rezum OR rezumTM OR nxthera OR (nx and thera) OR urolift OR prostatic urethral lift OR "Embolization, Therapeutic"[Mesh] OR embolization OR embolisation OR TUIP OR transurethral incision prostate OR TUMT OR transurethral microwave therapy OR aquablation OR TIND OR iTIND OR Nitinol OR robotic assisted prostatectomy OR "Transurethral Resection of Prostate"[Mesh] OR Transurethral Resection of Prostate OR TURP) Language limitations: articles in English, German and Italian will be included. Scientific literature will be monitored to check the availability of newly published RCTs that could be included. These will be eventually listed.

Table 2-4: Plan for data extraction

Planned data extraction and assessment of risk of bias
Evidence tables for data extraction will be created according to the Cochrane Handbook for Systematic Reviews of Interventions [9]. In the heading of the table the title of the review, the revision date (or version number) and the name (or ID) of the author that complete the table will be included. Information about data that will be extracted from the included studies are shown below: Author Year of publication Article ID Study ID (used in RevMan) Study Registration number (Registry identifier) Country/ies of recruitment Data collection period Funding sources Interventions Comparators Study design (RCT) Number of patients Inclusion criteria Exclusion criteria Number of patients in intervention group Number of patients in comparator group Patients age (mean) Prostate size or weight (mean, SD; median, range) Outcomes: effectiveness, intraoperative safety (general and technology-specific), postoperative safety (general and technology-specific), other outcomes Risk of Bias of RCTs

2.2.2. Project Scope

The EUnetHTA Guidelines, available at http://www.eunethta.eu/eunethta-guidelines, will be consulted throughout the assessment process. The Project Scope was discussed during the scoping e-meeting, attended by the assessment team and external experts. During the meeting, it was agreed to adopt the GRADE approach in order to finalize the list of outcomes and rate the importance of each outcome. The list of outcomes that resulted from the e-meeting was circulated among the panellists (assessment team and external experts) via the use of GRADEpro (https://gradepro.org/) .During a brainstorming phase; panellists reviewed the outcomes, added comments and/or added outcomes. The final list of outcomes was then circulated to the panellists, who were asked to rate the importance of each outcome, according to a 1 to 9 point scale ("1"

meaning the lowest importance and "9" meaning the highest importance). After completion of the rating round, the median of the votes was computed and each outcome was assigned a rate of importance: “critical” (median between 7 and 9); “important” (median from 4 to 6) and “not important” (median from 1 to 3). If medians were not integers the mean was considered. In Table 2-5 ratings of importance are reported for each outcome. Summary of Findings tables will be completed only for outcomes rated as “critical” and “important”.

According to guidelines, surgical approaches may be different depending on prostate size [1-2]; therefore the latter parameter will be used to define three relevant subpopulations often identified in guidelines (prostate size < 30 ml, 30 - 80 ml, > 80 ml or the same intervals measured as prostate weight in grams) which will be addressed by subgroup analyses, to provide more specific information on effectiveness and safety of the different techniques in each group of patients.

Since multiple comparisons will be performed through network meta-analyses, distinction between interventions and comparators in the following PICO should be considered indicative.

Table 2-5: Project Scope: PICO (please see HTA Core Model® for rapid REA)

Description	Project scope
Population	• The target condition is lower urinary tract symptoms (LUTS) attributed to non-neurological benign prostatic hyperplasia (BPH) (ICD-9 600.0; ICD-10 N40; MeSH term “Prostatic Hyperplasia”) • The target population is adult men (>18 of age) with LUTS attributed to BPH of non-neurological cause. • Either prostate weight or size will be used to define three relevant subpopulations often identified in guidelines (prostate size < 30 ml, 30 - 80 ml, > 80 ml or the same intervals measured as prostate weight in grams) which will be addressed by subgroup analyses *Rationale*: According to the guidelines [1-2] men with clinically significant LUTS attributable to BPH who do not find adequate relief with medical treatment or find side effects of medical treatment bothersome, may benefit from surgical treatment. Surgical treatment should be chosen for patients who: - did not improve after medical therapy, - do not want medical therapy but request active treatment (patient preference) - present with a strong indication for therapy (refractory urinary retention, renal insufficiency due to BPH, bladder stones, recurrent urinary tract infection, recurrent haematuria refractory to 5α-reductase-inhibitors).
Interventions	• Acquablation • Diode laser vaporization and diode laser enucleation • Holmium laser enucleation and holmium laser resection • Photoselective vaporisation with enucleation • Photovaporization (180W) • Plasmakinetik enucleation/resection • Prostate artery embolization (PAE) • Prostatic urethral lift (PUL) • Temporary implantable nitinol device • Thulium laser enucleation or vapoenucleation or vaporesection • Transurethral enucleation and resection • Transurethral enucleation with bipolar energy • Transurethral incision • Transurethral microwave therapy • Transurethral vaporization-electrovaporization • Water vapor therapy
Comparisons	• Transurethral resection of the prostate (TURP) • Prostatectomy or adenomectomy (OP)

Outcomes	**EFFECTIVENESS** • IPSS (International Prostate Symptom Score) • Qmax • PVR (post-void residual) • Reintervention • BPH Impact Index • Quality of life measures (generic) • Qmed • Persistent irritative symptoms (frequency, urgency, urge incontinence, nocturia) • Postoperative LUTS **SAFETY** **Intraoperative complications** • Procedural blood loss and transfusion requirements • Bladder perforation • Bladder and ureteral injury • Capsular perforation • Intraoperative mortality • Reduction of serum sodium **Intraoperative complications (technology-specific)** • Bowel injury (OP) • Rectal injury (OP) • Injury to adjacent structures (OP) • Incisional hernia (OP) • Vesico-cutaneous fistula (OP) • Epididymo-orchitis (OP) • Inadvertent embolisation of other sites (PAE) • Vascular thrombosis (PAE) • Pseudoaneurysms (PAE) • Dissection (PAE) • Damage of the perivascular, neural and muscular structures (PAE) • Haematomas (PAE) **Postoperative complications** • Erectile dysfunction or IIEF (International Index for Erectile Function) • Urinary incontinence • Catheterization time • TUR syndrome • Urethral stricture • Bladder neck contracture • Acute urinary retention • Urinary tract infection (clinical)

	• Retrograde ejaculation • Recatheterisation **Postoperative complications (technology-specific)** • Implant encrustation (PUL) • Migration rate of stent (PUL) • Radiodermatitis (PAE) **Other outcomes** • Hospitalization time • Procedure time
Study design	Randomized controlled trials (RCTs)

3. Communication and collaboration

Table 3-1: Communication

Communication Type	Description	Date	Format	Participants/ Distribution
Scoping	To internally discuss and reach consensus on the scoping	17.06.2020	E-meeting	Author(s), co-author(s), dedicated reviewers, , project manager, external experts
	Selection of outcomes and rating of importance of outcomes	22.06.2020	GRADEpro Software	Author(s), co-author(s), dedicated reviewers, external experts
First draft of the rapid assessment	To discuss comments of dedicated reviewers		E-meetings may be planned	Author(s), co-author(s), dedicated reviewers
Second draft of the rapid assessment	To discuss comments from ≥ 2 external experts		E-meetings may be planned	Author(s), co-author(s), dedicated reviewers, external experts

3.1 Dissemination plan

The final rapid assessment will be published on the EUnetHTA website: http://www.eunethta.eu/joint-assessments.

All stakeholders and contributors are informed about the publication of the final assessment by the project manager. Findings will be proposed for publication/presentation in relevant journals, conferences and databases.

3.2 Collaboration with stakeholders

Manufacturers of selected technologies will be involved only via a question-answer approach should the publicly available information on their websites prove insufficient to describe the technology in sufficient detail. Patients and/or patient organisations involvement will be attempted using the Open call for patient input issued on the EUnetHTA website. Patient organisations will be actively contacted to provide input about the disease and living with the disease.

3.3 Collaboration with EUnetHTA WPs

For the individual rapid assessment, some collaboration with other WPs is planned: WP7 [Implementation] will be informed of the project, in order to prepare activities to improve national uptake of the final assessment. Feedback on the WP4 REA process will be asked from the involved parties by WP6 [Quality Management], and this information will be processed by WP6 to improve the quality of the process and output.

3.4 Conflict of interest and confidentiality management

All authors, co-authors, dedicated reviewers, observers, external experts (health care professionals, patients or patient representatives) involved in the production of this assessment have declared they have no conflicts of interest in relation to the technology and comparator(s) assessed according to the EUnetHTA declaration of interest (DOI) form, which was evaluated following the EUnetHTA Procedure Guidance for handling DOI form (https://eunethta.eu/doi).

In case of involvement, manufacturer(s) will sign a Confidentiality Undertaking (CU) form regarding the specific project.

4. References

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5. Appendix A

5.1 Selected Assessment Elements

The table shows the assessment elements and the translated research questions that will be addressed in the assessment. They are based on the assessment elements contained in the 'Model for Rapid Relative Effectiveness Assessment'. Additionally, assessment elements from other HTA Core Model Applications (for medical and surgical interventions, for diagnostic technologies or for screening) have been screened and included/ merged with the existing questions if deemed relevant.

Table 5-1: Selected Assessment Elements

ID	Topic	Topic Issue	Relevance in this assessment [**Yes – critical**, **Yes** or **No**]	Mandatory (M) or non-mandatory (NM)	Research question(s) or reason for non-relevance of 'mandatory' elements
Description and technical characteristics of technology					
B0001	Features of the technology and comparators	What is the technology and the comparator(s)?	YES - critical	M	What are the various new minimally invasive and standard surgical approaches for BPH?
A0020	Regulatory Status	For which indications has the technology received marketing authorisation or CE marking?	YES - critical	M	For which indications have the different types of new minimally invasive surgical approaches for BPH received marketing authorisation or CE marking?
B0002	Features of the technology and comparators	What is the claimed benefit of the technology in relation to the comparator(s)?	YES - - critical	M	What is the claimed benefit of new minimally invasive surgical approaches for BPH in relation to the standard surgical approaches?
B0003	Features of the technology	What is the phase of development and implementation of the technology and the comparator(s)?	YES	NM	What is the phase of development and implementation of new minimally invasive and standard surgical approaches for BPH?
B0004	Features of the technology	Who administers the technology and the comparator(s) and in what context and level of care are they provided?	YES - critical	M	Who administers new minimally invasive and standard surgical approaches for BPH and in what context and level of care are they provided?
B0008	Investments and tools required to use the technology	What kind of special premises are needed to use the technology and the comparator(s)?	YES - critical	NM	What kind of special premises are needed to use new minimally invasive and standard surgical approaches for BPH?
B0009	Investments and tools required to use the technology	What equipment and supplies are needed to use the technology and the comparator(s)?	YES - critical	NM	What equipment and supplies (including maintenance resources) are needed to use new minimally invasive and standard surgical approaches for BPH?
E0001	Resource utilisation	What types of resources are used	YES	NM	What types of resources are used when using the different types of new

ID	Topic	Topic Issue	Relevance in this assessment [**Yes – critical**, **Yes** or **No**]	Mandatory (M) or non-mandatory (NM)	Research question(s) or reason for non-relevance of 'mandatory' elements
		when delivering the assessed technology and its comparators (resource-use identification)?			minimally invasive and standard surgical approaches for BPH?
A0021	Regulatory Status	What is the reimbursement status of the technology? [This assessment element can be placed either in the TEC OR in the CUR domain]	YES	NM	What is the reimbursement status of various new minimally invasive surgical approaches for BPH in the different EU countries?
Health problem and current use of technology					
A0002	Target Condition	What is the disease or health condition in the scope of this assessment?	YES - critical	M	What is the type of BPH in the scope of this assessment?
A0003	Target Condition	What are the known risk factors for the disease or health condition?	YES - critical	NM	What are the known risk factors for BPH?
A0004	Target Condition	What is the natural course of the disease or health condition?	YES - critical	M	What is the natural course of BPH?
A0005	Target Condition	What are the symptoms and the burden of disease or health condition for the patient?	YES	M	What are the symptoms and the burden of BPH for the patient?
A0006	Target Condition	What are the consequences of the disease or health condition for the society?	YES	NM	What are the consequences of BPH for the society?
A0024	Current Management of the Condition	How is the disease or health condition currently diagnosed according to published guidelines and in practice?	YES - critical	M	How is BPH currently diagnosed according to published guidelines and in practice?
A0025	Current Management of the Condition	How is the disease or health condition currently managed according to published guidelines and in practice?	YES - critical	M	How is BPH currently managed according to published guidelines and in practice?
A0007	Target Population	What is the target population in this assessment?	YES - critical	M	What is the target population in this assessment?
A0023	Target Population	How many people belong to the target population?	YES	M	How many people belong to the target population?
A0011	Utilisation	How much are the technologies utilised?	YES	M	How much are the new minimally invasive surgical approaches for BPH utilised?
Clinical effectiveness					
D0001	Mortality	What is the expected	NO	M	The different techniques are expected

ID	Topic	Topic Issue	Relevance in this assessment [**Yes – critical**, **Yes** or **No**]	Mandatory (M) or non-mandatory (NM)	Research question(s) or reason for non-relevance of 'mandatory' elements
		beneficial effect of the intervention on mortality?			to impact on functional outcomes and quality of life rather than mortality
05	Morbidity	How does the technology affect symptoms and findings (severity, frequency) of the disease or health condition?	YES - critical	M	How do interventions with new minimally invasive surgical approaches for BPH compare to standard surgery approaches in terms of Qmax, Qmed, PVR, IPSS, BPH Impact Index and quality of life?
D0006	Morbidity	How does the technology affect progression (or recurrence) of the disease or health condition?	YES - critical	M	How do interventions with new minimally invasive surgical approaches for BPH compare to standard surgery approaches in terms of retreatment rate and persistent LUTS / irritative symptoms ?
D0011	Function	What is the effect of the technology on patients' body functions?	NO	M	Addressed in D0005
D0016	Function	How does the use of technology affect activities of daily living?	NO	NM	Addressed in D0005 + D0012
D0012	Health-related quality of life	What is the effect of the technology on generic health-related quality of life?	YES	M	How do interventions with new minimally invasive surgical approaches for BPH compare to standard surgical approaches in terms of patient reported outcomes and general quality of life?
D0013	Health-related quality of life	What is the effect of the technology on disease-specific quality of life?	YES - critical	M	What are the effects of new minimally invasive surgical approaches for BPH compared to standard surgical approaches on disease-specific quality of life?
D0017	Patient satisfaction	Were patients satisfied with the technology?	YES	NM	How do interventions with new minimally invasive surgical approaches for BPH compare to standard surgical approaches in terms of patient satisfaction?
Safety					
C0008	Patient safety	How safe is the technology in relation to the comparator(s)?	YES - critical	M	How safe are new minimally invasive surgical approaches for BPH compared to standard surgery approaches in terms of intraoperative and postoperative complications?
C0002	Patient safety	Are the harms related to dosage or frequency of applying the technology?	NO	NM	Dosage is not an issue applicable to this technology.
C0004	Patient safety	How does the frequency or severity of harms change over time or in different settings?	YES	M	How safe are new minimally invasive surgical approaches for BPH compared to standard surgery approaches over time or in different settings of use?
C0005	Patient safety	What are the susceptible patient groups that are more likely to be harmed through the use of the	YES - critical	M	What are the susceptible patient groups that are more likely to be harmed through the use of new minimally invasive surgical approaches for BPH?

ID	Topic	Topic Issue	Relevance in this assessment [**Yes – critical**, **Yes** or **No**]	Mandatory (M) or non-mandatory (NM)	Research question(s) or reason for non-relevance of 'mandatory' elements
		technology?			
C0007	Patient safety	Are the technology and comparator(s) associated with user-dependent harms?	YES - critical	NM	How do interventions with new minimally invasive surgical approaches for BPH compare to standard surgery approaches in terms of user-dependent harms (i.e.time of surgical procedure, complications etc.)?
B0010	Safety risk management	What kind of data/records and/or registry is needed to monitor the use of the technology and the comparator(s)?	YES	M for medical devices NM for screening and diagnostics	What kind of data/records and/or registry is needed to monitor the use of new minimally invasive and standard surgical approaches for BPH?

5.2 *Checklist for potential ethical, organisational, patient and social and legal aspects*

1. Ethical	
1.1. Does the introduction of the new technologies and their potential use/non-use instead of the defined, existing comparator(s) give rise to any new ethical issues?	Yes
Equity of access issues	
1.2. Does comparing the new technologies to the defined, existing comparators point to any differences that may be ethically relevant?	No
The comparators are widely available.	
2. Organisational	
2.1. Does the introduction of the new technologies and their potential use/non-use instead of the defined, existing comparator(s) require organisational changes?	Yes
The new interventions require substantial additional resources.	
2.2. Does comparing the new technologies to the defined, existing comparator(s) point to any differences that may be organisationally relevant?	Yes
3. Social	
3.1. Does the introduction of the new technologies and their potential use/non-use instead of the defined, existing comparator(s) give rise to any new social issues?	No
3.2. Does comparing the new technologies to the defined, existing comparator(s)	No

point to any differences that may be socially relevant?	
4. Legal	
4.1. Does the introduction of the new technologies and their potential use/non-use instead of the defined, existing comparator(s) give rise to any legal issues?	No
4.2. Does comparing the new technologies to the defined, existing comparator(s) point to any differences that may be legally relevant?	No

6. APPENDIX B.

Rating of outcomes after the survey among the project participant (using the GRADEpro tool)

Functional outcomes – quality of life	**Rate of importance**
IPSS	9 (6-9) - critical
Qmax	8.5 (2-9) - critical
PVR	8 (2-9) - critical
Reintervention	7.5 (6-9) - critical
BPH Impact Index	7 (1-9) - critical
Quality of life measures (generic)	6.5 (2-9) - critical
Qmed	4.5 (1-8) - important
Intraoperative complications	**Rate of importance**
Procedural blood loss and transfusion requirements	7 (5-9) - critical
Bladder perforation	7 (4-9) - critical
Bladder and ureteral injury	6 (4-9) - important
Capsular perforation	6 (5-9) - important
Intraoperative mortality	6 (3-9) - important
Reduction of serum sodium	4 (2-7) - important
Haemoglobin alteration	3 (2-8) - not important
Intraoperative complications (technology-specific)	**Rate of importance**
Bowel injury (OP)	7 (2-8) - critical
Rectal injury (OP)	7 (2-8) - critical
Injury to adjacent structures (OP)	6.5 (2-8) - important
Inadvertent embolisation of other sites (PAE)	6 (2-8) - important
Vascular thrombosis (PAE)	6 (2-9) - important
Incisional hernia (OP)	6 (2-9) - important
Pseudoaneurysms (PAE)	5 (2-7) – important
Dissection (PAE)	5 (2-9) – important
Damage of the perivascular, neural and muscular structures (PAE)	5 (2-8) - important
Vesico-cutaneous fistula (OP)	5 (2-8) - important
Epididymo-orchitis (OP)	4.5 (2-8) - important
Haematomas (PAE)	4 (2-6) - important
Vascular access (PAE)	3 (2-6) - not important
Postoperative complications	**Rate of importance**
Erectile dysfunction	8.5 (7-9) - critical
Urinary incontinence	8 (7-9) - critical
Catheterization time	7 (1-9) – critical
TUR syndrome	7 (5-9) – critical
Urethral stricture	7 (4-9) – critical
Bladder neck contracture	7 (5-9) - critical
Acute urinary retention	7 (5-9) - critical
Urinary tract infection	7 (3-9) - critical
Retrograde ejaculation	7 (5-9) - critical
Persistent irritative symptoms	6.5 (1-9) - critical
Recatheterization	6.5 (3-9) - important
Postoperative LUTS	5.5 (1-9) - important
Long-term mortality	3.5 (1-9) not important
Postoperative complications (technology-specific)	**Rate of importance**
Implant encrustation (PUL)	6 (2-7) - important
Migration rate of stent (PUL)	6 (2-8) - important
Radiodermatitis (PAE)	4 (2-6) – important
Other outcomes	**Rate of importance**
Hospitalization time	8 (5-9) - critical
Procedure time	6 (3-9) - important